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AN OUTBREAK OF ASEPTIC MENINGITIS ASSOCIATED WITH ECHO VIRUS TYPE 4

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The group of enteric cytopathogenic human orphan (ECHO) viruses, described in 1955 by the Committee on the ECHO Viruses,[1] at present comprises 19 types. Some of these have been obtained from the stools of healthy children;[1-3] a number have been isolated from the stools of patients with the clinical syndrome of aseptic or non-bacterial meningitis, in the absence of additional evidence of an aetiological relationship to the disease;[4] and several have been shown to be the probable causes of illness in man.

ECHO virus type 2 has been isolated from the spinal cord of a fatal case of bulbo-spinal paralysis resembling poliomyelitis.[5, 6] Several investigators have recovered type 6 from the alimentary tracts of patients with aseptic meningitis,[7-10] a rise in neutralizing antibody occurring in most of the cases. Type 9 has been associated with outbreaks of aseptic meningitis in which a number of patients developed a rash on the face, trunk and limbs, virus being recovered from cerebrospinal fluid[11-13] as well as from the throat and from stools,[14-16] while a rise in neutralizing antibody has been demonstrated. Type 4 has been described in association with an epidemic of aseptic meningitis in Marshalltown, Iowa, in 1955, the virus being recovered from 21 of 57 stools tested and from 2 of 7 throat washings. One cerebrospinal fluid was tested and found to be negative.[17, 18]

The present paper describes the isolation of ECHO virus type 4 from 10 of 18 children investigated during an outbreak of aseptic meningitis in an institution in Johannesburg, the virus being found in the cerebrospinal fluids of 7 patients and in the stools of 3.

Clinical Features

In the first 3 months of 1957 a high proportion of children in the Johannesburg Children's Home developed a syndrome characterized by pyrexia, severe frontal headache, vomiting and neck stiffness. During the earlier half of January all the children were absent on vacation with their relatives or friends. On 16 January 2 siblings returned, one of them becoming ill 5 days later. On 24 January the rest of the children returned, and within 3 days 2 developed a similar illness. In the succeeding 6 weeks, 58 out of a total of 121 children had become affected. The incubation period would appear to be short, 3 days having elapsed between the first and the next 2 cases, while during the following 9 days 38 other children developed the syndrome.

The Home was divided into 2 units, one for 30 infants and the other for 91 older children. These groups were not in direct contact with each other, the only links being the kitchen and the adult staff. The older children first became involved, and a period of 20 days elapsed before the infants were affected. During this time an adult nurse developed the illness, and it is possible that she conveyed the infection to the infants. Arthropod transmission was at first considered, and some mosquitoes were inoculated into tissue cultures without success. The subsequent recovery of virus from stools and the pattern of incidence suggest that a person-to-person transmission was operative.

The onset of illness was usually sudden. Pyrexia of 100-102°F and severe frontal headache were common, while nausea and vomiting occurred in more than half the cases. Neck and back stiffness, with or without a positive Kernig's sign, was present in the more severe cases, but tendon reflexes were normal and weakness was absent. Muscle tenderness was not a prominent feature, but was occasionally observed. Some children complained of photophobia or painful eyes, and suffusion of the conjunctivae was noted in a few. The illness was mild in the majority of cases, persisting for a few

days only. A notable feature was the tendency to relapse, with identical clinical findings, observed in 10 children; 5-10 days elapsed between recrudescences; one child had 2 relapses while another had 3.

Sixteen children were admitted to the Johannesburg Fever Hospital for further investigation. Two of these showed, in addition to the common signs, moderately enlarged spleens and tender cervical, axillary and inguinal lymph nodes. One had a palpable liver, with mild disturbance of hepatic function as reflected in biochemical serum tests. Blood counts on these 2 cases showed predominance of lymphocytes, with atypical forms present; but the Paul-Bunnell tests were negative. Neck and back stiffness was present, and in both cases there was pleocytosis in the cerebrospinal fluid, virus being obtained from the fluid of one (J.S.).

Laboratory Investigations

Cerebrospinal fluids from 18 cases, taken shortly after admission to hospital, usually between the 1st and 3rd days of illness, were examined. In 2 instances the fluid was normal, but one of these patients (F.B.) was carrying virus in the stool. In the other 16 fluids pleocytosis was the chief abnormality. Lymphocytes occurred in a range of 5-150 per c.mm. and predominated in 10 fluids; while polymorphonuclear leucocytes occurred in a range of 0 to 610 per c.mm., and predominated in 6. In 5 fluids the protein values (34 to 55 mg. per 100 ml.) were slightly above the upper limit of normal (30 mg. per 100 ml.). Sugar and chloride estimations fell within the normal ranges, and no bacteria could be detected.

A polymorphonuclear leucocytosis (10,000-19,000 per c.mm.) was found in the blood of 8 of 17 patients, but the counts were otherwise not markedly altered, with the exception of the 2 cases showing atypical lymphocytes, one of whom (J.S.) had a lymphocytosis of 22,700 per c.mm.

Other routine laboratory investigations included the Paul-Bunnell test and complement-fixation tests for leptospira, rickettsiae, and the viruses of herpes simplex, mumps and lymphocytic choriomeningitis; all of which were negative.

VIRUS ISOLATION

Monkey kidney roller tube cultures, prepared from fresh trypsinized renal epithelium of the vervet monkey *Cercopithecus aethiops pygerythrus* were grown in a medium containing 0·5% lactalbumin hydrolysate in Hanks' salt solution and 5% horse serum. Just before inoculation the fluid was changed, with the omission of serum; and every 4-5 days the medium was renewed, with the addition of 0·5% horse serum.

Human amnion roller tube cultures, prepared from fresh trypsinized membranes, were grown in a medium consisting of Parker medium no. 199 with 20% human serum. Before inoculation and at subsequent fluid renewals the medium was changed to Parker no. 199 or 0·5% lactalbumin hydrolysate in Hanks' salt solution with 0·5-2% horse serum.

Strain HeLa human malignant epithelial cells, kept in continuous cultivation since 1954, when they were received from Dr. G. O. Gey of Baltimore, were grown in a medium consisting of Parker No. 199 with 0·025% Difco yeastolate, 0·05% lactalbumin hydrolysate, and 30% human serum. Before inoculation and at subsequent fluid changes they received a medium consisting of Parker No. 199 with 2% horse serum.

Specimens from 18 patients in the acute phase of illness were tested in tissue cultures for the presence of virus as soon after collection as possible, in a number of cases less than an hour elapsing before inoculation. All tissue cultures were incubated at 36-37°C.

Blood. 0·3-0·5 ml. samples of whole blood from 3 patients were inoculated into kidney cultures, which were then observed for 24-33 days without cytopathic changes becoming apparent. Included here were patients F.B., who had virus in the stool, and C.M., whose cerebrospinal fluid contained virus.

Throat Swabs. Swabs from 5 patients were agitated in 1-2 ml. of Hanks' salt solution containing antibiotics, and the fluids were inoculated into kidney cultures, which were observed for 24-27 days without cytopathic changes being noted. Of these patients, C.M. had virus in the cerebrospinal fluid, while M.B. and C.H. carried virus in their stools.

Rectal Swabs. Rectal swabs were agitated in 1-2 ml. of Hanks' solution containing antibiotics, and the fluid was centrifuged at 3,000 r.p.m. for 30 minutes before being inoculated in 0·25 ml. amounts into each of 3 kidney culture tubes. Swabs from 7 patients were examined, and from 3 (F.B., M.B., C.H.) virus was obtained. Negative cultures were observed for 27-33 days, and there was no evidence of virus on blind passage.

Cerebrospinal Fluid. Kidney cultures were inoculated with cerebrospinal fluids from 16 children, 0·15-0·25 ml. being put into each of 3 tubes for each patient, and virus was recovered from 7 (B.C., S.F., Y.F., J.G., C.M., A.S. and J.S.). Two patients whose cerebrospinal fluids were negative had virus in the stool (F.B., M.B.). The recovery of virus from the fluid of C.M. was successfully repeated; re-isolation not being attempted in the other cases.

Viral behaviour in tissue culture

Cytopathic effects in kidney cultures became apparent in primary isolations between the 7th and 19th days after inoculation, and prompt passage of undiluted fluid resulted in the complete destruction of cultures within 4 days. In a number of instances harvested culture fluid was stored for 5-9 weeks at −20°C, with a resultant marked drop in infectivity until further passage restored the titre. Titrations of strains showed levels ranging from $10^{4.5}$ to $10^{6.75}$ TCID50 (doses infective for 50% of the tissue cultures) per 0·1 ml.

No cytopathic changes were seen over periods of 11-16 days when human amnion cultures were inoculated with 10^4 and 10^5 TCID50 of strain C.M., although kidney cultures inoculated in parallel were completely destroyed by the 4th day. Strain A.S. was also inoculated into amnion and kidney cultures in parallel, the former showing no changes over 20 days, while the kidney cultures were completely destroyed by the 6th day. Rectal swab suspensions and cerebrospinal fluids which proved to be positive for virus in kidney cultures were inoculated in parallel into amnion cultures during the original isolation attempts, with negative results.

HeLa cell cultures were inoculated with the C.M. strain on 2 occasions and observed for 7 and 9 days without cytopathic effect. Kidney cultures inoculated in parallel showed complete destruction by the 4th day.

Monkey kidney cover-slip cultures lying free in roller tubes were inoculated with 6 strains of virus, fixed with Bouin's solution, and stained with haematoxylin and eosin. Early changes included eosinophilic staining of the nucleus, and the appearance of a paranuclear zone which stained a deeper red than the rest of the cytoplasm. Later, the nucleus became folded or scrolled, and was laterally displaced by the enlarged paranuclear zone, which now stained less intensely than the remaining cytoplasm. Finally the cells became shrunken and rounded, with dense cytoplasm and small dark nuclei. No inclusions were observed.

VIRUS IDENTIFICATION

(a) Neutralization Tests

Strain C.M. was chosen as the prototype, and was tested against immune sera for ECHO virus types 1-16, 18 and 19 which had been kindly supplied by Dr. A. B. Sabin of Cincinnati and Dr. J. L. Melnick of New Haven. Antiserum for type 17 was not available. Three rabbit sera prepared in our laboratories for the 3 types of poliovirus were also included. An estimated challenge dose of 100 TCID50 was mixed with an equal volume of inactivated serum diluted 1 in 10 to give a final serum dilution of 1 in 20, for inoculation into each of 3 kidney cultures after being held at 4°C for 1 hour. Tubes read at the 8th day showed complete destruction except where sera for ECHO types 4, 18 and 19 and Polio types 1, 2 and 3 had been used. The protection by sera for ECHO types 4 and 18 and for Polio 1 and 3 was complete;

ECHO type 19 serum protected 1 tube fully and 2 tubes partially; while Polio type 2 serum protected 2 tubes fully and 1 tube partially.

Neutralization by the protecting sera was re-tested, with the use of a challenge of 1,000 TCID50 as measured in a parallel titration, and the cultures were observed for 7 days. Control cultures inoculated with the challenge dose only were entirely destroyed by the 5th day; complete protection was given by ECHO type 4 serum; while a slow break-through occurred where sera for ECHO types 18 and 19, and for Polio types 1, 2 and 3 were used.

The ECHO and Polio sera which gave partial protection against strain C.M. were all derived from rabbits, and the possibility exists that a neutralizing factor resistant to inactivation at 56°C for 30 minutes against strains of ECHO virus type 4 may be encountered in rabbits.

The 10 strains isolated were then tested with a monkey antiserum to ECHO type 4 produced under the auspices of the Committee for ECHO viruses and sent to us by Dr. H. A. Wenner of Kansas City. The dried serum was diluted 1 in 5, inactivated at 56°C for 30 minutes, cooled, and mixed with an equal volume of virus suspension estimated to contain 100 TCID50 per 0·1 ml., giving a final serum dilution of 1 in 10. This was held at 4°C for 1 hour, and then 0·2 ml. amounts of each serum-virus mixture were inoculated into each of 4 kidney culture tubes. Uninoculated control tubes were set up, together with 3 tubes inoculated with the virus challenge dose only, for each strain tested. The cultures were incubated at 36°C, and were read on the 3rd and subsequent days. Neutralization was considered to have occurred when all control tubes inoculated with virus only showed cytopathic effect involving the entire culture and no change was present in the tubes inoculated with serum-virus mixture. Further readings were taken at least 24 hours later to check that protection had been maintained. By these criteria, all the 10 strains were neutralized by the ECHO type 4 serum.

At the same time, the serum in a final dilution of 1 in 50 was tested against each strain. In every instance it failed to protect at this dilution. The serum was stated to have a neutralizing titre of 30-75 against 32-200 TCID50, which is conspicuously lower than that of sera produced by the same workers against the rest of the first 13 ECHO viruses. At a final reading of the neutralization test on the 7th day, 6 strains showed a late break-through in occasional tubes, protection in all 4 tubes persisting for the other 4 viruses. It is felt that the failure of the 1 in 50 serum dilution and the partial late break-through in some instances was due to the initial low titre of the antiserum.

(b) Filtration

Tissue culture fluid containing strain C.M. was filtered under 2-3 lb. pressure through a membrane filter having an estimated maximum pore diameter of 450 millimicra and an average pore diameter of 275 millimicra. Both pre- and post-filtration fluids produced complete destruction of kidney cultures within 3 days. The culture fluid was immediately followed by a suspension of *Serratia marcescens* in buffered saline under pressure of 5 lb. The pre-filtration suspension produced a profuse growth on coagulated serum medium within 48 hours, but no bacteria could be detected in the post-filtration fluid.

(c) Ether

Tissue culture fluid containing strain C.M. was centrifuged at 3,000 r.p.m. for 30 minutes and the supernatant fluid was divided into two aliquots. To one, ether was added up to a quarter of the total volume, while the other sample was held as a control. Both were kept at 4°C for 24 hours, and were well shaken several times during that period. Titration after 24 hours showed that the unetherized sample contained over 10^8 TCID50 per 0·1 ml., while the etherized sample contained $10^{5.5}$ per 0·1 ml.

(d) Mice

Litters, each comprising 6 infant white mice approximately 24 hours old, were inoculated with undiluted tissue culture fluid. Two litters were inoculated by the combined intraperitoneal-subcutaneous route, and one litter by the intracerebral route, with strain C.M. No clinical signs of disease were noted during the observation period of 21 days, and histological examination of one mouse from each litter taken on the 10th day showed no lesions. Strain F.B. was also inoculated into similar litters by the same routes, and no signs of disease were detected.

Eight 4-5-week-old white mice were inoculated intracerebrally with strain C.M., and showed no signs of illness over 21 days.

Tissue culture controls of all inocula demonstrated the presence of virus.

(e) Rabbits

Two rabbits given 4 intravenous inoculations of undiluted tissue culture fluid containing strain C.M. for the purpose of producing immune serum showed no signs of illness.

Neutralization with paired sera

In Table I are given the results of a neutralization test using 316 TCID50 of strain C.M. against acute- and convalescent-phase sera from 4 patients. In each case the virus produced obvious cytopathic changes by the 3rd day when tested with acute-phase sera; but convalescent-phase sera consistently delayed the appearance of changes for at least 24 hours, suggesting the presence of a low level of antibody.

TABLE I. ACUTE- AND CONVALESCENT-PHASE SERA CHALLENGED WITH 316 TCID50 OF STRAIN C.M.

Serum (final dilution 1 in 2)	*Tubes showing cytopathic changes on days*		
	3	4	5
M.B. February 6	3/3		
March 12	0/3	3/3	
V.G. February 18	3/3		
March 9	0/3	2/3	3/3
C.H. February 6	3/3		
March 12	0/3	2/3	3/3
A.L. February 6	3/3		
March 12	0/3	2/3	3/3

DISCUSSION

It is clear that ECHO virus type 4 is a poor antigen for the production of neutralizing antibodies. This is shown not only by the low titre of the monkey antiserum, but also by the findings of Chin *et al.*,[18] who noted that in their series of patients the rise of antibody was slow, did not exceed a low level, and was absent in 2 cases with aseptic meningitis. It is therefore probable that evidence of neutralizing antibody rise between paired sera will be difficult to demonstrate when clinical cases of ECHO type 4 infections are encountered. This would seem to eliminate one of the most valuable proofs of aetiology, and some other indication of immunity or a more sensitive test may have to be sought. Poor antibody formation may account for the striking incidence of relapses, and another immunity mechanism may determine recovery particularly where the course of the disease is short.

In the present series of cases, isolation of virus from the cerebrospinal fluids of patients with the syndrome of aseptic meningitis should suffice to confirm the causal relationship, in the absence of marked antibody rise.

Only 7 rectal swabs were examined in the present investigation, 3 being positive. It is felt that if stools had been taken, a higher isolation rate would have been achieved, since another unit in these Laboratories at the same time was investigating stools from the Fever Hospital for poliovirus, and recovered non-polio viruses not yet further characterized from the stools of 3 patients in our series who had virus in

their cerebrospinal fluids. Faecal contamination would account readily for the manner in which infection spread through the institution in which the outbreak occurred.

The selective affinity of this virus for monkey kidney cells contrasts with the behaviour of ECHO type 9, which grows better on human amnion[18] and is pathogenic for infant mice. This serves to demonstrate that the successful isolation of viruses necessitates the use of a variety of tissues.

SUMMARY

During an outbreak of aseptic meningitis in a children's institution in Johannesburg in 1957, a virus resembling ECHO virus type 4 was isolated from the cerebrospinal fluids of 7 patients and from the rectal swabs of 3 other patients.

A marked rise in the neutralizing antibody content of convalescent-phase sera tested did not occur, and it is suggested that this might account for the relapses noted in the outbreak.

The virus was isolated in tissue cultures of monkey kidney, and did not produce cytopathic changes in cultures of human amnion or HeLa cells.

We wish to thank Dr. J. W. Scott-Millar, Medical Officer of Health for Johannesburg, for allowing us to investigate these cases; Dr. A. L. Jackson, Physician-in-Charge of the Fever Hospital, for permission to consult records; and Dr. R. Brueckner and Dr. E. Chesler for collecting specimens. The cooperation of the Matron and staff of the Johannesburg Children's Home in facilitating the investigations is gratefully acknowledged. We also thank Dr. J. H. S. Gear, Director of the Poliomyelitis Research Laboratories, for the encouragement he has given to us during this study.

REFERENCES

1. Committee on the ECHO Viruses (1955): Science, **122**, 1187.
2. Ramos-Alvarez, M. and Sabin, A. B. (1954): Proc. Soc. Exp. Biol., **87**, 655.
3. Honig, E. I., Melnick, J. L., Isacson, P., Parr, R., Myers, I. L. and Walton, M. (1956): J. Exp. Med., **103**, 247.
4. Habel, K., Silverberg, R. J. and Shelokov, A. (1957): Ann. N.Y. Acad. Sci., **67** (art. 8), 223.
5. Steigman, A. J., Kokko, U. P. and Silverberg, R. J. (1953): Amer. J. Dis. Child., **86**, 509.
6. Steigman, A. J.: Personal communication cited in Karzon *et al.*[8]
7. Davis, D. C. and Melnick, J. L. (1956): Proc. Soc. Exp. Biol., **92**, 839.
8. Karzon, D. T., Barron, A. L., Winkelstein, W. and Cohen, S. (1956): J. Amer. Med. Assoc., **162**, 1298.
9. Kibrick, S., Melendez, L. and Enders, J. F. (1957): Ann. N.Y. Acad. Sci., **67** (art. 8), 311.
10. Meyer, H. M., Rogers, N. G., Miesse, M. L. and Crawford, I.P. (1957): *Ibid*, **67** (art. 8), 332.
11. Boissard, G. P., Stokes, L. J., Macrae, A. D. and MacCallum, F. O. (1957): Lancet, **1**, 500.
12. Quersin-Thiry, L., Nihoul, E. and Dekking, F. (1957): Science, **125**, 744.
13. Nihoul, E., Quersin-Thiry, L. and Weynants, A. (1957): Amer. J. Hyg., **66**, 102.
14. Crawford, M., Macrae, A. D. and O'Reilly, J. N. (1956): Arch. Dis. Childh., **31**, 182.
15. Tyrrell, D. A. and Snell, B. (1956): Lancet, **2**, 1028.
16. McLean, D. M. and Melnick, J. L. (1957): Proc. Soc. Exp. Biol., **94**, 656.
17. Lehan, P. H., Chick, E. W., Doto, I. L., Chin, T. D., Heeren, R. H. and Furcolow, M. L. (1957): Amer. J. Hyg., **66**, 63.
18. Chin, T. D., Beran, G. W. and Wenner, H. A. (1957): *Ibid.*, **66**, 76.

BOOKS RECEIVED : BOEKE ONTVANG

Anaesthesia for Nurses. By Eric Godwin, L.R.C.P., M.R.C.S., F.F.A.R.C.S. Pp. 98. 12 Figures. 9s. 6d. + 6d. postage. Bristol: John Wright & Sons Ltd. 1957.

The Public Health Inspector's Handbook. A Manual for Public Health Officers. Ninth Edition. (Completely Revised.) By Henry H. Clay, F.R.S.H., F.I.P.H.E., assisted by Ronald Williams, O.B.E., D.P.A., F.R.S.H. Pp. xx + 614. 101 Illustrations. £2 0s. 0d. net. London: H. K. Lewis & Co. Ltd. 1957.

Hewers's Text-book of Histology for Medical Students. Seventh Edition. Edited by C. L. Foster, M.Sc., Ph.D. Pp. viii + 438. 418 Figures. 27s. 6d. net. London: William Heineman, Medical Books Ltd. 1957.

Sekretionsstudien am Pankreas. Experimentelle und anatomische Pathologie. Von Priv.-Doz. Dr. V. Becker. VI + 120 Seiten. 54 zum Teil mehrfarbige Abbildungen in 77 Einzeldarstellungen. Kartoniert DM. 29.50. (Zwanglose Abhandlungen aus dem Gebiet der normalen und pathologischen Anatomie, Herausgegeben von Prof. Dr. W. Bargmann und Prof. Dr. W. Doerr, Heft 1). Subskriptionspreis für Bezieher der gesamten Reihe DM 23.60. Stuttgart: Georg Thieme Verlag. 1957.

The Doctor's Signature. By Hamilton Johnston. Pp. 255. 13s. 6d. London: Victor Gollancz Ltd. 1957.

Hospital in the Bush. By E. W. Doell. Pp. 216. 9 Illustrations. 18s. net. London: Christopher Johnson Publishers Ltd. 1957.

The Diagnosis and Treatment of Infections. By D. Geraint James, M.A., M.D. (Cantab.), M.R.C.P. (London). Pp. viii + 234. 30s. Oxford: Blackwell Scientific Publications. 1957

The Clinical Application of Antibiotics. Volume III. Chloramphenicol and the Tetracyclines. By M. E. Florey, M.D. Pp. ix + 303. 23 Figures. 84s. London: Oxford University Press. 1957.

Artificial Insemination in the Human. By A. M. C. M. Schellen, M.D., with an introduction by Sophia J. Kleegman, M.D. Pp. xii + 420. 10 Illustrations and 35 Tables. 72s. Amsterdam Houston London. New York: Elsevier Publishing Company. 1957.

Sir Robert W. Philip, 1857-1939. Memories of his Friends and Pupils. Edited by Harley Williams. Pp. 96. 4 Illustrations. 12s. 6d. London: National Association for the Prevention of Tuberculosis. 1957.

A Handbook on Diseases of Children—Including Dietetics and the Common Fevers. Eighth Edition. By Bruce Williamson, M.D. (Edin.), F.R.C.P. (Lond.). Pp. xi + 483. 27s. 6d. net + 1s. 6d. postage abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1957.

The Epidemiology and Control of Malaria. By George Macdonald, C.M.G., M.D., F.R.C.P. Pp. xv + 201 + xl + 11. 17 Illustrations. 30s. London: Oxford University Press. 1957.

Anesthesia: A Manual for Students and Physicians. Fifth Edition. By Stuart C. Cullen, M.D. Pp. 295. 37 Figures. $5.50. Chicago: Year Book Publishers, Inc. 1957.

Surgery: A Guide to Surgical Diagnosis and Treatment including Tropical Surgery. The Oxford Handbooks for Medical Auxiliaries. By W. G. Kerr, M.B., F.R.C.S. (Ed.). Pp. viii + 410. 25s. London: Oxford University Press. 1957

Cunningham's Manual of Practical Anatomy. Twelfth Edition. Volume I. General Introduction, Upper Limb, Lower Lmb., Revised by James Couper Brash, M.C., M.A., M.D., D.Sc., LL.D., F.R.C.S. (Ed.), F.R.S.E. Pp. xii + 394. 196 Figures 25s. London: Oxford University Press. 1957.

The Disease of Tobacco Smoking and Its Cure. By Lennox Johnston, M.B., Ch.B. (Glasgow), with a Foreword by Marcus Lipton, O.B.E., M.A., J.P., M.P. Pp. 104. Illustrations. 3s. 6d. London: Christopher Johnson Publishers Ltd. 1957

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VAN DIE REDAKSIE

DIE GEVARE VAN ANTIBIOTIESE BEHANDELING

Om ons hoofartikel van verlede week oor die antibiotika voort te sit, wil ons nou verwys na die newe-effekte van hierdie soort behandeling. As ons in aanmerking neem dat die antibiotika oor die hele wêreld gebruik word, is dit veelbetekenend dat ernstige stoornisse as gevolg van hulle grootskaalse gebruik nog maar baie selde aangemeld is. Daar is egter heelwat newe-uitwerkings wat, ten spyte van die feit dat sommige dokters hulle as minder belangrik beskou, nogtans baie werklik is en die pasiënt veel ongemak kan besorg. Daar is party antibiotiese middels wat veranderings in die liggaam kan veroorsaak wat later in kwaai reaksies kan ontwikkel. Die langtermyn risiko's sal natuurlik eers na jarelange noukeurige bestudering en nagaan van gevalle bereken kan word.

Van die twyfelagtige gebruike van antibiotika, word die aanwending van penisilliensalf vir velbesmettings afgekeur omdat dit geneig is om 'n allergie te veroorsaak—'n ongewenste gevaar by 'n middel soos penisillien wat soveel nuttige gebruike het. Ook by die gebruik van dié oogsalf vir karkaatjies en ooglidontsteking is daar ook gevaar dat plaaslike reaksies kan ontstaan. Gewone penisillien-inspuitings kan ook die gevaar inhou dat gevoeligheid ontstaan as die behandelingskursus dikwels herhaal word. Maar hierdie feite moet egter nie die geneesheer afskrik van die gebruik van penisillien by gevalle waar dit aangewese is nie. Waar dit bevind word dat 'n organisme gevoelig is vir penisillien sowel as vir ander antibiotiese middels, word penisillien gewoonlik verkies omdat dit selfs in die grootste dosisse baie veiliger is om toe te dien. Penisillien het die spesiale voortreflikheid dat dit ewe maklik in klein as in groot dosisse toegedien kan word.

By streptomisien ontwikkel bakteriese weerstand baie gou, hoewel dit vertraag of voorkom kan word in gevalle van die tuberkelbasil deur die gesamentlike gebruik van die tuberkulostatiese middels wat vandag in die mode is. Vergiftigende effekte (sien hieronder) kan die nuttigheid van hierdie middel beperk, maar kom vandag minder dikwels voor danksy die skedule van behandeling wat uitgewerk is; dan ook sal hulle oor die algemeen eers voorkom nadat die middel miskien baie weke aaneen toegedien is.

Sekere soorte stafilokokke wat bestand is teen penisillien word vandag goed uitgeken. 'n Mens kom hulle meer dikwels in hospitale as in die algemene praktyk teë. Baie soorte is bestand teen die tetrasikliene en eritromisien, en ander organismes soos pseudomonas en proteus begin ook nou dieselfde neiging toon. Dit word nou voorgestel dat die nuwe antibiotika soos oleandomisien, novobiosien en spiramisien gebruik word by die behandeling van infeksies met gram-

EDITORIAL

HAZARDS IN ANTIOBIOTIC THERAPY

In continuation of last week's editorial on antibiotics we pass on to refer to the side-effects of this form of therapy. Considering the world-wide use of antibiotics it is significant that very few serious disturbances have been reported from their wholesale use. There are, however, numerous side-effects which, though regarded by some doctors as minor troubles, are nevertheless very real in nature and cause much discomfort to the patient. Some may evoke changes in the body that may suddenly develop into severe reactions at a later time. The long-term risks will naturally only be evaluated after years of careful study and follow-up.

Amongst doubtful uses of antibiotics, the application of penicillin ointment for skin infections is condemned as being likely to lead to allergy, an undesirable risk for a drug so widely useful as penicillin; the eye ointment for styes and blepharitis also carries danger of local reactions. Ordinary injections of penicillin may also lead to sensitization if the courses are frequently repeated. These considerations ought not to deter doctors from using penicillin in cases where it is indicated. Where an organism is found to be sensitive to penicillin as well as to other antibiotics, penicillin is usually the drug of choice, being far safer to give, even in the highest dosage. The special advantage of penicillin is that it is just as easy to give a huge dose as one of conventional size.

With streptomycin, bacterial resistance develops rapidly, although this can be delayed or prevented in the case of the tubercle bacillus by the combined use of the tuberculostatic drugs now in vogue. Toxic effects (see below) may limit the usefulness of this drug, but they occur less frequently nowadays with the schedules of treatment that have been developed, and are not generally likely to appear until perhaps the drug has been continuously given for many weeks.

Penicillin-resistant strains of staphylococcus are now well recognized. They are found more often in hospitals than in general practice. Many strains are resistant to the tetracyclines and erythromycin, and other organisms, e.g. pseudomonas and proteus, are showing the same trend. Newer antibiotics such as oleandomycin, novobiocin and spiramycin are being proposed for the treatment of infections with gram-positive cocci resistant to penicillin and other antibiotics.

Bacitracin, polymyxin and neomycin are generally too

positiewe kokke wat weerstand bied teen penisillien en ander antibiotika.

Bacitrasien, polimiksien en neomiksien is oor die algemeen te toksies vir sistemiese gebruik; hulle kan die niere en die VIIIste harsingsenuwee beskadig.

Wat die vergiftigingseffekte van die antibiotiese middels betref, kan 'n paar punte beklemtoon word. Penisillien is vandag die algemeenste oorsaak van anafilaktiese skok; daar is verslae van meer as 200 ernstige gevalle en meer as 50 sterfgevalle; dit is nie bekend hoeveel nooit gerapporteer is nie. Die reaksie kan onmiddellik plaasvind (miskien met die dood as gevolg) of dit kan vertraag wees. Dit volg soms op mondelikse toediening maar meer dikwels op spier-inspuitings. Noodhulpmiddels behoort altyd byderhand te wees—adrenalien, aminofillien, antihistamien, hidrokortisoon, klaar vir inspuiting. Dit word gemeen dat 'n mens nie op die antihistamiene kan vertrou om die reaksies te voorkom nie. Veltoetse is nie betroubaar nie. Afgesien van hierdie kwaai dog ongewone soort reaksie, is daar ander wat nie so ernstig is nie, maar wat meer dikwels voorkom. Die nuwe fenoksiemetiel penisillien vir mondelikse toediening kan effense buikkrampe, vloeibare stoelgange, en apteuse mondvliesontsteking veroorsaak, en dit het ook reeds reaksies van oorgevoeligheid teweeggebring.

Daar is meer kans dat voorkamerstoornisse soos vertigo en ataksie by streptomisien voorkom as by dihidrostreptomisien, wat aan die ander kant stoornisse van die oor, byvoorbeeld tinnitus en doofheid, veroorsaak wat selfs progressief kan ontwikkel nadat die behandeling al gestaak is. Sommige gesaghebbendes het al heeltemal opgehou met dihidrostreptomisien omrede sy uitwerking op die gehoororgane. Afgesien van hierdie spesiale stoornisse wat by 'n lang behandeling voorkom is allergiese reaksies, wat ernstig kan wees, glad nie seldsaam nie.

Om van die wye-spektrum antibiotika te praat: Chloramfenikol is geneig om aplastiese anemie en agranulositose te veroorsaak, maar ons weet nog nie hoe dikwels dit gebeur nie. Hierdie uitwerkings kom blykbaar meer dikwels by vroumense as by mans voor. Die plaaslike aanwending van chloramfenikol op die oë en vel kan reaksies van oorgevoeligheid veroorsaak. Al die wye-spektrum antibiotika, veral die tetrasikliene wat so dikwels gebruik word, veroorsaak stoornisse van die maagdermkanaal. Hierdie stoornisse is gewoonlik nie ernstig nie maar kom nogal dikwels voor. Die uitbarstende ontsteking van die maag, dun- en dikderm is gelukkig seldsaam. Die swambestrydende middel mikostatien is beskikbaar vir 'n bykomende besmetting met *Candida albicans*, wat somtyds ontstaan na lang behandeling met hierdie middel. Roetine voorbehoedingsbehandeling met hierdie middel, bv. saam met tetrasiklien, is onwenslik omdat mikostatien-bestande candida-soorte kan ontwikkel, en omdat ander organismes soos *Proteus vulgaris* later die botoon kan begin voer. Allergiese stoornisse kan soms volg op behandeling met die wye-spektrum antibiotika en herhaalde plaaslike aanwending veroorsaak soms reaksies van oorgevoeligheid.

Robson, J. M. en Keele, C. A. (1956): *Recent Advances in Pharmacology*. Londen: Churchill.
Beckman, H. (1956-57): Year Book of Drug Therapy. Chicago: The Year Book Publishers.

toxic for systemic use; they may damage the kidney and the eighth cranial nerve.

As regards toxic effects produced by antibiotics a few points should be emphasized. Penicillin has become the commonest cause of anaphylactic shock; over 200 serious cases and more than 50 deaths have been reported; how many are not recorded is unknown. The reaction may be immediate, perhaps fatal, or delayed. It may follow oral, but more likely intramuscular, administration. An emergency kit should always be at hand—adrenaline, aminophylline, antihistamine, hydrocortisone, ready for injection. It is believed that antihistaminic drugs cannot be relied on to prevent reactions. Skin testing is not reliable. Apart from this severe but uncommon type of reaction there are others of relatively minor nature that occur more frequently. The recently introduced phenoxy-methyl penicillin for oral administration can produce slight abdominal cramp, liquid stools, and aphthous stomatitis, and has also produced reactions of hypersensitivity.

With streptomycin, vestibular disturbances, e.g. vertigo and ataxia, are more likely to occur than with dihydrostreptomycin which, on the other hand, is more prone to produce auditory disturbances, e.g. tinnitus and deafness, which may even develop progressively after treatment has been stopped. Some authorities have given up dihydrostreptomycin altogether because of the auditory effects. Apart from these special disturbances that occur with prolonged therapy, allergic disturbances are not infrequent, and may be severe.

Turning to the wide-spectrum antibiotics, chloramphenicol is liable to cause aplastic anaemia and agranulocytosis, the true incidence of which remains to be determined. These effects apparently occur more commonly in females. Local application of chloramphenicol on eye and skin may produce sensitization reactions. All wide-spectrum antibiotics, especially the extensively used tetracyclines cause gastrointestinal disturbances. These are generally of mild degree but not uncommon. Fulminating gastro-entero-colitis is fortunately rare. For *Candida albicans* superinfection that may occasionally arise after prolonged administration of these antibiotics, the antifungal agent mycostatin is available. The routine prophylactic use of this agent, e.g. in combination with tetracycline, is not considered advisable because mycostatin-resistant strains of candida may develop, and because other organisms such as *Proteus vulgaris* may come to predominate. Allergic disturbances occasionally follow the administration of the wide-spectrum antibiotics, and repeated local application sometimes leads to sensitization reactions.

Robson, J. M. and Keele, C. A. (1956): *Recent Advances in Pharmacology*. London: Churchill.
Beckman, H. (1956-57): *Year Book of Drug Therapy*. Chicago: The Year Book Publishers.

THE ANCESTRY OF MEDICINE

The true ancestor of modern medicine was not a person like the witch-doctor of primitive races of today but the priest-physician of the civilizations which existed at the dawn of history. It was in Sumeria that there lived the earliest representatives of this profession about whom archeological information is available. There in the Land of the Two Rivers nearly 6,000 years ago, sat physicians who wrote down case-records and prescribed medicines. Copies of their prescriptions have been found in cuneiform tablets at Ur, at Gilgamesh and at Erech.

Possibly an idea of how these Sumerian priest-doctors worked can be gained from the writings of Herodotus, who described the procedure as it existed in his day, nearly 2,500 years later. The patient was taken into a large waiting space near the temple and market place and was set down on one of the matting beds so common in the Near East even to the present day. In this concourse of the sick, passages were left where the passer-by could walk and observe the individual patient. If anyone knew of a suitable remedy, it was his privilege to inform the priest, who might thus be assisted in his treatment—a procedure faintly foreshadowing the multiple consultations of today.

The progress made in European medicine during the last two centuries or so should not blind us to the fact that in India and in China progress in the art continued at about the same pace as in Europe for hundreds of years, and that until the 18th century there was very little to choose between oriental and western medicine. This is only to be expected, for they both sprang from the same source, viz. the priest-doctors of Sumer. The history of western medicine is relatively clear—from Sumeria to Egypt, from Egypt to Greece, from Greece to Rome, and thence to medieval and modern Europe. The Indian and Chinese genealogy, however, remained very obscure until recently. It is only in the last decade that a completely lost civilization coeval with that of Sumer has been uncovered in the valley of the Indus. The work of Sir Mortimer Wheeler in digging out the ruins and elucidating their implications has traced the link between Sumer and the ancient civilizations of India and the Far East. These civilizations and that of Europe ran neck and neck through the middle ages and the early Renaissance until 400 years ago.

It should be chastening to reflect that in the two great peninsulas of Asia, viz., Europe and India, scientific development and medical progress proceeded at about the same pace until so recently. At the Renaissance an explosive development of science and art found expression in Europe, which from that time took the lead it retains to the present day; but even as late as the early 19th century Mokerji of Bombay, the great Indian lithotomist, was as skilful and successful a surgeon as Civiale of Paris and Cheselden of England who lived at about the same time. It was only the industrial revolution and the development of technology that gave the West the propellant whose momentum carries it ever further ahead even to this day.

It we are in search of the first medicine-man we need look no further than the primitive witch-doctor; but the true ancestor of modern medicine was the priest-physician.

Thorwald, J. (1957): *The Century of the Surgeon.* London: Thames and Hudson.

CANCELLOUS BONE GRAFTS

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Some time ago no special attention was paid to the structure of bone grafts. The immediate strength of the graft seemed to have been the decisive argument for the choice of the appropriate material. When Job-a-Meck'ren in 1670 in Amsterdam had to cover a defect of the skull, reported to be the first successful bone transplantation in medical history, he used a corresponding piece of bone from the skull of a dog. At the turn of the century the experiments of Ollier and Wolff were repeated and studied histologically, particularly by Barth (1894) and Axhausen (1909).

Much of the information then gained is still the basis of our present concepts; all grafted bones with or without periosteum become necrotic, are resorbed and become replaced by creeping substitution (*schleichender Ersatz*) if they are in contact with a osteogenic bed. The treatments by Lexer and his co-workers during and after World War I was based on this theory.

Not much attention was paid to the findings of Partsch (1922), who reported that contrary to leading opinion a complete survival of cancellous grafts was possible. He had removed and examined iliac bone grafted to the mandible 3 weeks after operation in a patient who had died from pneumonia. No regressive changes could be detected. Partsch concluded that the theories about the healing of bone grafts should be revised.

This was confirmed by Matti in 1932, who proved in animals that homologous cancellous chips—placed in a suitable diaphyscal bed—can survive transplantation. He recommended small chips for the treatment of cystic bone deformities and false joints.

Homologous iliac grafts have been shown by plastic surgeons to be superior to tibial grafts primarily for architectural reasons (Dick 1946, Higgs 1946, Martin 1948), but various investigators and clinicians have noted that the cancellous grafts are not reabsorbed as quickly as cortical grafts (Zenker, 1946).

All depends on the speed of revascularization. Cancellous structure affords abundant avenues for an easy and quick invasion of blood vessels and for fluid exchange (Siffert, 1955). Assuming that the new bone does not form around the grafted cancellous chips as a result of the activity of the bed but arise from the surviving surface cells of the graft, Ham and Gordon (1955) studied the survival of cancellous bone in dogs. They considered that those chips which are

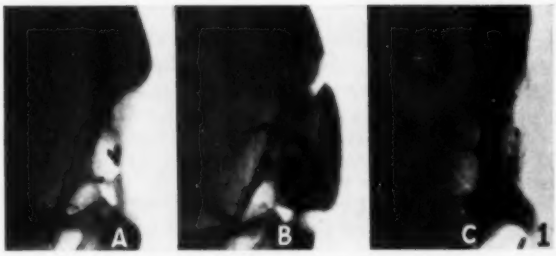

Fig. 1. X-ray taken (*a*) before operation, showing defect; (*b*) immediately post-operative, showing graft *in situ*; (*c*) 5 years later, showing absorption of graft.

required to form new centres of osteogenesis should be placed in close contact with a tissue where there are capillaries to supply tissue fluid to the surface cells. Contrary to Lentz (1955), they found that the difference in the healing process between a fresh and a preserved graft is fundamental. In none of 5 dogs did new bone form in association with chips thrice frozen and thawed. But in all of 5 dogs new bone did form in association with untreated chips.

In this conflict of opinions we wanted to learn to what extent the bone grafts in our patients become necrotic, reabsorbed and substituted, or survived, and also what sort of grafts would be most suitable in certain cases.

When, as recommended by Lexer, during and after the war, we selected periosteum-covered thick tibial grafts for

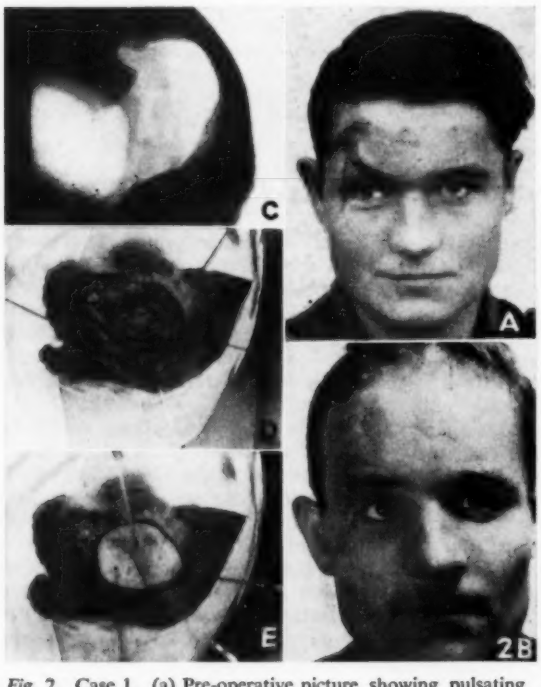

Fig. 2. Case 1. (a) Pre-operative picture showing pulsating defect in skull in frontal area. (b) Post-operative. (c) X-ray showing defect. (d) and (e) Manner of replacing and fixing bone.

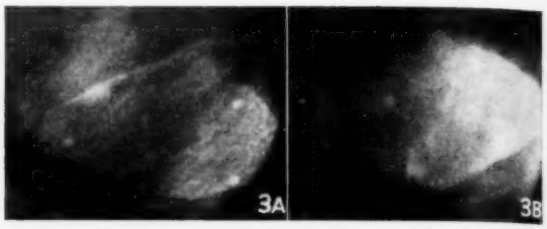

Fig. 3*a*. Skull replacement *in situ*
Fig. 3*b*. 5 years later, showing absorption.

the repair of forehead bone defects (Fig. 1), we found that these grafts were in fact being absorbed. A substitution or a survival of the periosteal layer occurred only to a minimal extent. The very thin bony shell 5 years after grafting is just strong enough to support the contour of the face (Fig. 1c).

CASE 1

The more easily obtainable preserved homografts give a similar result. A pulsating frontal defect in a young woodcutter was covered with a boiled piece of skull derived from a neurosurgical operation on another patient. This graft was fixed with a periostal margin from the bed. Three months later the graft was partly reabsorbed not only at the edges but also from inside as demonstrated by the enlargement of the drill holes (Fig. 3). Five years later only a very thin bone shell remains, which protects the brain from chance pressure but possibly not from injuries. The homograft was chosen because it was uncertain whether the closure would cure the traumatic epilepsy; fortunately it did.

CASE 2

Because of the earlier experiences we changed to iliac grafts with at least one cancellous surface. In this case (Fig. 4) a small but pulsating forehead defect had to be covered in a 16-year-old girl. She was an expert skier but had crashed on a rock during a race. She was restored nicely, but in spite of the good fitting of the graft, absorption went on and after 5 years only tiny bony remains could be seen of what should have been a firm cover for the frontal lobe.

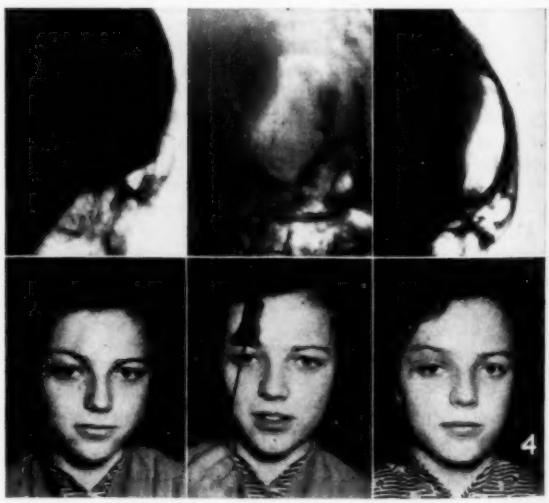

Fig. 4. Case 2. Series showing pre- and post-operative appearance after forehead defect has been replaced.

CASE 3

In case 3 a large piece was necessary to repair a defect which was suffered by a goalkeeper in a soccer game (Fig. 5). Since the nasal bone had to be restored too, an extra piece of bone with a cancellous surface was impaled on the shaped graft. We

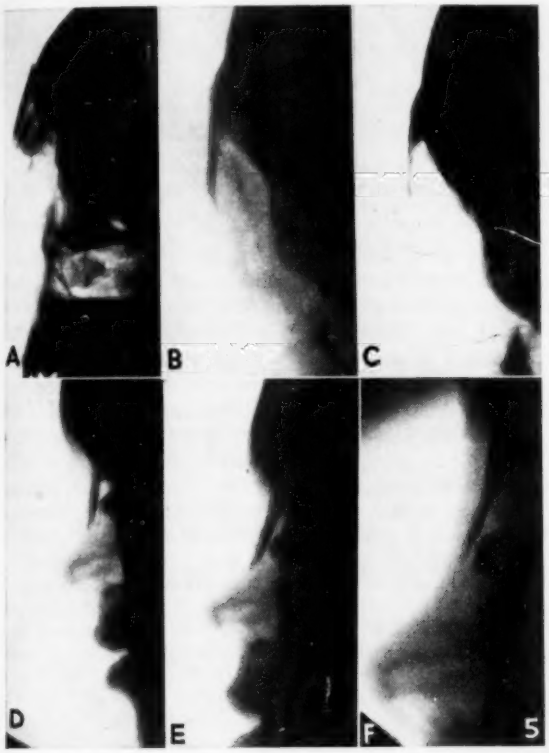

Fig. 5. Case 3. Series of X-ray pictures showing gradual absorption of replaced nasal bones. (*a*) and (*d*) Immediately post-operative. (*b*) and (*e*) 1 year later. (*c*) and (*f*) 5 years later.

thought the large cancellous surface which was fitted tightly to the scarred but highly vascularized surface of the frontal lobe of the brain would enable the graft to survive to a large extent. After 1 year the graft was markedly reabsorbed (Fig.5b). After 5 years (Fig. 5c) the graft was well healed to the skull but the take was poor. It is interesting to note that the nasal part of this graft has taken quite well and has retained a mass of bone similar to a nasal bone after 5 years.

The fluid exchange and vascularization in the nose seems to be sufficiently good for the survival of small cancellous grafts. We could observe a good take in most of our patients and, since cartilage may become reabsorbed in the nose to a remarkable extent, the use of cancellous bone is advisable for nose reconstruction.

CASE 4

This 16-year-old girl (Fig. 6) with a congenital nose deformity was treated with a forehead rhinoplasty and a cancellous graft from the iliac crest. The X-ray pictures 5 years later shows that most of the graft had taken.

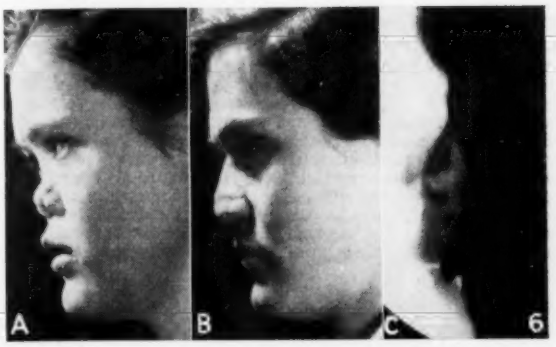

Fig. 6. Case 4. (*a*) Congenital nose deformity. (*b*) After forehead rhinoplasty and cancellous graft. (*c*) Showing bone graft in position.

If cancellous chips are transferred to the gluteal muscle they become completely necrotic, and are reabsorbed (Seyfarth 1954, Siffert 1955). If they are grafted to the nose as in atrophic rhinitis they remain almost unchanged. We believe that cancellous bone, widely accepted as the best material for repair of the nose, is not the material of choice for smaller forehead defects and for the orbital margin. Here we prefer diced cartilage to bone. The bulk of the 2 mm. cubes is not reabsorbed, at least not to an extent

Fig. 7. Case 5. (*a*) Series showing pre-operative forehead defect. (*b*) Showing defect filled. (*c*) 5 years later.

which could be noted clinically, whereas a remarkable reabsorption takes place as a rule with solid pieces of cartilage especially in the orbital region.

CASE 5

In a patient who was treated with diced cartilage because of a gunshot wound of the face (Fig. 7) we noted that the supra-orbitally grafted cartilaginous mass had grown to a pea-sized chondroma-like tumour, which we had to cut out a year after operation. The photograph taken 5 years after operation shows that the mass of cartilage cubes retained its size and smooth surface perfectly. The only additional treatment required with this method is to apply a plaster mould over the grafted region for 10 days.

In repair of the hand cancellous bone has also been used for many years. If one impales the cancellous phalangeal substitute right into the metacarpal or phalangeal capitulum an immediate communication between the spongy venous sinuses seems to take place. The graft may heal within several weeks just as a metaphyseal fracture may heal. No necrotic changes have occurred up to now but functional adaptation has taken place on the surface as well as in the

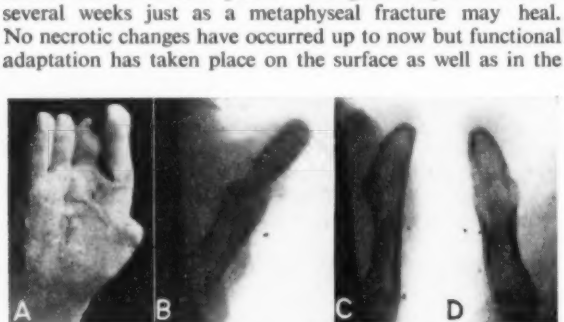

Fig. 8. Case 6. Cancellous bone used to lengthen amputated thumb (a).(b)-(f): Showing progressive solidification of graft with apparent development of a cortical layer.

interior. A cortical layer and a marrow cavity form and in case 6 (a boy) it looks (Fig.8) as if the graft had grown with the hand in 5 years.

Autotransplanted phalanges from an otherwise lost or sacrificed less important finger have also been regarded as ideal material for finger reconstruction. When Nicoladoni of Innsbruck, who is reported to have succeeded for the first time in thumb reconstruction, in 1896 saved a denuded thumb by a pedicle graft from the breast, he was lucky to have the blood supply of the bone still intact. This achievement of plastic surgery was so extraordinary at the time that nobody, not even the patient and his relatives, bothered about the nipple which was accidently transferred with the pedicle flap to the thumb too.

Nicoladoni had no success with tibial grafts in two consecutive cases of thumb reconstruction. He therefore proposed a finger exchange operation and subsequently the ingenious method of transferring the toes to the hand.

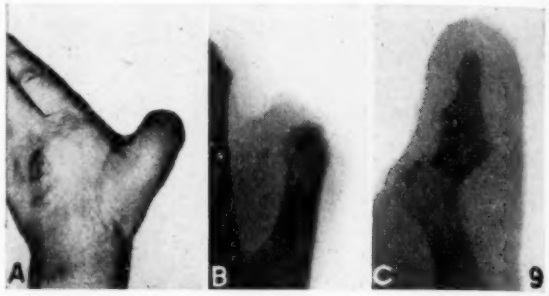

Fig. 9. Case 7. (*a*) Showing amputated thumb. (*c*) Showing bone graft using freely grafted phlanges. (*b*) 5 years later, showing almost complete reabsorption.

Sir Harold Gillies (1940) proposed autografting amputated fingers because he thought that no living tissue which can possibly be preserved should be wasted. Advised by Gillies, in 1952 we autografted the amputated thumb in 4 patients (Wilflingseder 1952) and learned that freely grafted phalanges also obey the law of necrosis, reabsorption and creeping replacement the same as cortical bone grafts. There is no surface for quick fluid exchange and revascularization. Our attempts in regrafting amputated thumbs have not been very successful. In case 7 the thumb shown in Fig. 9, in spite of poor sensation and stiffness, is a good working finger for the 40-year-old carpenter and has enabled him to earn his living. But the autografted thumb was painful for several months, progressive reabsorption took place in the

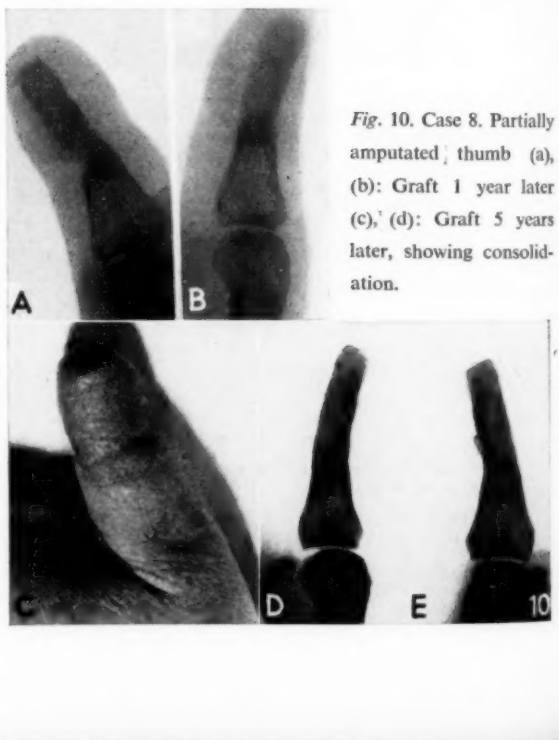

Fig. 10. Case 8. Partially amputated thumb (a), (b): Graft 1 year later (c), (d): Graft 5 years later, showing consolidation.

bone, the nail plate disappeared, and little of the original shape remained.

If there is no possibility of restoring sensation and mobility we would rather recommend to do away with an amputated phalanx or a very seriously destroyed bone in a compound fracture and replace it by a phalangeal graft carved out from the iliac crest.

CASE 8

In a 30-year-old carpenter a graft (Fig. 10) was applied underneath a cross-arm flap to restore the important finger to its full length which he had partly lost on a machine. The take was a complete one and the man returned to his workshop 6 weeks later. The X-ray picture one year later shows that a cortical layer has already been formed and the length of the graft has not diminished. When the graft was carved a small hump was left. One can see that hump still unchanged after one and after 5 years (Figs. 10d, 10e). This clinical observation again makes us believe that this cancellous bone has completely survived grafting.

From practical experiences we may conclude that cancellous iliac grafts should be widely used in hand and face reconstruction.

REFERENCES

Axhausen, G. (1909): Arch. klin. Chir., **88**, 23.
Dick, I. G. (1946): J. Bone Surg., **28**, 1.
Ham, A. and Gordon, St. (1953): Brit. J. Plast. Surg., **5**, 154.
Gillies, H. (1940): Lancet, 1002.
Idem (1951): Personal communications.
Higgs, S. L. (1946): J. Bone Jt. Surg., **28**, 15.
Job-A-Meek'ren (1682): *Observat. med. chir. Ex Belgico*, Latin trans. ab. A. Blasion Amstelodami, p. 6. Lentz.
Lentz, W. (1955): *Die Grundlagen der Transplantation von fremden Knochengewebe*. Thieme, Stuttgart.
Lexer, E. (1924): *Die freien Transplantationen*, Neue Dtsch. Chir., 26.
Maatz, R., Lentz, W. and Graf, R. (1952): J. Bone Jt. Surg., **36**, 721.
Matti, H. (1932): Arch. klin. Chir., **168**, 236.
Martin, H. (1948): Surgery, **24**, 103.
McEwen, W. (1912): *The Growth of Bone*, Glasgow. Quoted by Lentz.
Nicoladoni, C. (1897): Wien. klin. Wschr., Nr. 28.
Ollier, L. (1880): Verhandl. Intern. Med. Kongress, Berlin.
Partsch, F. (1922): Zbl. Chir., **49**, 989.
Seyfarth, H. (1953): *Ibid.*, **78**, 323.
Siffert, R. (1955): J. Bone Jt. Surg., **37A**, 742.
Wilflingseder, P. (1952): Arch. orthop. Unfall-Chir., **45**, 617.
Wolff, J. (1863): Langenb. Arch., **4**, 183.
Zenker, R. (1946): Chirurg, **17**, 339.

METASTASIZING ARGENTAFFINOMA FROM THE DERMATOLOGIST'S POINT OF VIEW

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The relationship between dermatology and general medicine has, during the last two decades, become much closer than it ever was before and internists are finding the assistance of dermatologists useful in the detection of many visceral diseases. We have only to recall the large number of criminals eventually tracked down by the clues they leave in the skin, for example, the papulonecrotic tuberculide which uncovers the cause of a pyrexia of unknown origin; the Raynaud's phenomenon or the sudden, symmetrical, dusky erythema which exposes acute systemic lupus erythematosus; the generalised pruritus which may be the first symptom of Hodgkin's disease; and the localised pruritus vulvae which leads to the discovery of glycosuria in diabetes mellitus.

The dermatologist is now coming to the aid of the general physician in the diagnosis of the peculiar and interesting carcinoid syndrome, first described only 5 years ago by Biörck[1] and Thorson,[2] and independently by Isler and Hedinger,[3] and by Rosenbaum, Santer and Claudon.[4] The earliest and most obvious manifestation of the syndrome is a strange flushing which leads some menopausal female patients to seek gynaecological advice, but which is most likely to confront the dermatologist who must be aware of the syndrome and its diverse symptomatology, for no other disease produces quite the same cutaneous changes.[5,6,7]

The carcinoid syndrome is fascinating not only to the dermatologist but to the surgeon who finds the primary argentaffin tumours in the gastro-intestinal tract and their metastases in the liver, mesenteric lymph nodes, lungs, kidneys, adrenals, retroperitoneal tissues, gallbladder, stomach, pancreas and brain,[8] and occasionally in the ovaries,[13] bones, spleen, heart, thyroid and epididymis;[34] to the cardiologist who detects the tachycardia and the right-sided valvular abnormalities, pulmonary stenosis and tricuspid incompetence, which may lead to failure with oedema and ascites;[9,10] to the allergist who finds bronchospasm, expiratory stridor and 'asthma' in some of the patients; to the gastro-enterologist who investigates the explosive diarrhoea associated with borborygmi and increased peristalsis;[11,12,13] to the psychiatrist who may be consulted about certain mental aberrations[13-17] and to the biochemist and histopathologist who are finding the activities of the chromaffin cells and their secretions extremely interesting.

In 1914, Gosset and Masson (cited by MacDonald)[16] demonstrated that the Kultschitsky cells of the crypts of Lieberkühn were the cells of origin of carcinoid tumours and pointed out the similarity between the tumour cells and paraganglial chromaffin tissue. They were the first to suggest that argentaffin tumours were endocrine in nature.

In 1948, Rapport, Green and Page[18] isolated from beef serum a single substance, different from epinephrine, tyramine, histamine and tryptamine, which appeared during the clotting or defibrination of blood and which had a vasoconstrictor effect. They showed it to be an indole derivative chiefly present in platelets. This was serotonin.

Erspamer,[19] working independently, discovered the same substance and named it 'enteramine', believing that it was produced by the chromaffin cells of the gastro-intestinal tract. He found it to have three main functions: it plays a part in haemostasis, it is intimately concerned with normal

mental function and it is an important factor in the maintenance or depression of normal arteriolar tone.

Lembeck[20] extracted serotonin from carcinoid tumours in 1953. The substance serotonin or enteramine is now known as 5-hydroxytryptamine (5-HT). It is manufactured by chromaffin cells from the basic substance tryptophan and it travels from the tumours to the lungs, where most of it is converted into a pharmacologically inactive substance, 5-hydroxyindole acetic acid (5-HIAA), by the action of mono-amino oxidase. The maximum content of 5-HT is present in the blood only during its brief passage from the liver through the right side of the heart to the lungs whence it emerges as 5-HIAA.[6,9]

Apart from Kierland's[21] recent patient who was found to have a functioning primary argentaffinoma in an ovarian teratoma with no evidence of any metastases, the carcinoid syndrome has manifested itself only in cases with extensive secondary deposits, mainly in the liver.[6,13,22,25] The flushing persists after removal of the primary tumour.[23] There are, however, cases of metastasising argentaffinomas with no flushing or other features of the syndrome.[11]

Branwood and Bain[29] suggest that in the carcinoid syndrome, hepatic dysfunction produced by metastases and cardiac cirrhosis may prolong the action of 5-HT by delaying its breakdown to 5-HIAA. In normal people a little 5-HIAA is found in the urine, but it is enormously increased in carcinoidosis and may be detected by simple tests.[11,13,23,24,26,27,28]

The physiological and pharmacological properties of 5-HT are by no means fully understood. It does appear to have a profound effect on smooth muscle, leading to bronchospasm, increased intestinal peristalsis, hypertrophy of the pulmonary artery and strange vasomotor phenomena in the cutaneous blood vessels.

Although 5-HT is a vasoconstrictor, its actions on the circulation are complex, with hyper- or hypotensive or mixed responses.[25] Intradermal injection of 5-HT produces local congestion and venous spasm.[13] Artificial raising of the serotonin level in the blood does not produce the syndrome,[11] though some blushing and tingling may occur, and serotonin antagonists fail to influence the flushing. As Erspamer remarks, this drug has a 'perverse pharmacological record'.

Page,[33] attempting to explain the mixed vasomotor actions of 5-HT, which may at times be pressor and at other times depressor, uses the term 'amphibaric' to describe these effects. The initial quick fall in blood pressure noted after an injection of 5-HT is due to vasodilation which probably depends on a temporary ganglion-blocking mechanism.

Some workers postulate that the flushing in the carcinoid syndrome is due to a secondary release of histamine.[6,27,31] It has been shown that 5-HT does in fact liberate histamine from living tissue, particularly from platelets during clotting.[31] Daugherty *et al.*[32] found, on the other hand, that intravenous histamine led to an outflow of 5-HT from carcinoid tumours and drew an analogy between this and the release by histamine of pressor amines from phaechromocytomas. Antihistaminics, however, have no effect on the course and duration of the flushes in the carcinoid syndrome. Radioactive gold (^{198}Au) has been found to control the symptoms by temporarily counteracting a naturally occurring mono-amino oxidase inhibition.[9]

Serotonin has been found to be present in the chromaffin cells of the gastro-intestinal tract, in the suprarenal glands, the central nervous system, the spleen, the liver and the lungs; it is also present in the serum and urine. It is transported by the platelets in the blood to the tissues. Mast cells have very recently been shown to contain 5-HT as well as histamine and heparin, and histamine-liberators release both histamine and 5-HT from mast cells in connective tissue.[35-42]

Chromaffin cells and mast cells both contain granules but, whereas the granules in chromaffin cells have been shown to be formalin artefacts,[30] those of the mast cells actually carry heparin, histamine and 5-HT which are liberated when the granules disintegrate.[43] Mast cells are found in connective tissues, particularly of the dermis and the panniculus; they are most numerous in the papillary layer of the dermis and around capillary beds and are arranged in concentric circles around walls of small blood vessels, appearing to arise from perivascular cells which are indistinguishable from fibroblasts.[44] They are enormously increased in urticaria pigmentosa which is now regarded as a mastocytosis and which may occasionally be accompanied by a histamine type of flushing.[45]

CUTANEOUS MANIFESTATIONS

Cutaneous manifestations which have been seen in association with malignant argentaffinoma consist of vasomotor phenomena, pellagrinous dermatoses, palmar and plantar erythema, neurodermatitis, vitiligo and acropachyderma.

The cutaneous vasomotor picture in the carcinoid syndrome is unique, though in its early stages it may be confused with the menopausal 'hot flushes' of middle-aged women. Malignant argentaffinomas tend to afflict men and women in the middle decades of life; by far the youngest recorded cases are Biörck's original patient, a youth aged nineteen years, and a boy of fifteen recently described by Becker.[46]

The vascular symptoms may be of a transient or a lasting nature,[34] but evanescent attacks of flushing which have been likened by Bean[5] to 'the fickle phantasmagory of the Aurora Borealis' are the most characteristic features of the syndrome.

A typical flush may be spontaneous or it may be precipitated by alcohol, cheese, seasoned foods, heat, emotion, standing, or manipulation of the lower bowel by enemata. It always starts with a subjective hot feeling and a redness of the face, quickly followed by the appearance of brick-red spots on the limbs. After two or three minutes the face becomes paler and the brick-red spots may disappear or, if the flush is going to last longer, they may become larger with interspersed blue areas, looking like 'lakes on a map', according to Waldenström and Ljungberg.[34] The picture now is one of a macular, patchy, purple cyanosis alternating with some areas of great pallor and others of a brick-red colour, nearly always confined to the face, neck and extremities, and leading to an appearance terrifying to the patient and to all who behold him. The flush may last 7 or 8 minutes and is usually accompanied by strong heart palpitations, tachycardia, bronchospasm and diarrhoea. 'Goose flesh' may be seen and is due to temporary contraction of the arrectores pilorum muscles.

The different colours in the skin represent various stages in contraction and dilation of the small cutaneous vessels. According to Roddie *et al.*,[50] an injection of 5-HT into the brachial artery leads to constriction of the vessels in the forearm and hand which produces a great resistance to the

flow of blood; this, in turn, causes a dilatation of superficial vessels and marked flushing of the skin. Sapeika[15] postulates a central action of 5-HT on the diencephalon as a possible cause of the flushing.

Bean, Olch and Weinberg[5] 'can see no real resemblance of the clinical features of this syndrome to the crises of phaechromocytoma, the vasomotor storm of thyrotoxicosis, the mottled flush of the diencephalic hypertensive or diencephalic epilepsy, the unilateral flush-sweat of Madam Frey's syndrome or the unilateral burst of flushing seen in very young infants'.

Waldenström, Pernow and Silwer[23,27] have evinced great interest in a patient who for many years has had a histamine type of flushing associated with tachycardia and with large amounts of histamine and 5-HT in her blood and urine. Roentgenograms reveal widespread sclerotic foci in the bones, but neither mast cells nor argentaffin cells are seen in bone biopsies. Though no mast cell infiltrations are found in the bones, it is tempting to think that she is, in fact, suffering from systemic urticaria pigmentosa. Subcutaneous histamine given to this patient induces a flush which differs from that of carcinoidosis in its longer duration and its consistently bright red colour without cyanosis. It is possible that the histamine flushes last longer than those caused by 5-HT because histamine is destroyed more slowly than 5-HT in the tissues. Waldenström *et al.* suggest that the same enzyme in argentaffin tumour cells may produce both histamine and 5-HT from different precursors. Histamine is formed from histidine and 5-HT from tryptophan, both by a process of decarboxylation. Excess of histamine as well as of 5-HT is found in the urine of patients with carcinoidosis. It is well known that histamine may produce flushing without the other usual accompaniments of urticaria, itching, headache and stimulation of gastric secretion.[27]

Later, in spite of a rapidly developing tolerance to 5-HT, so great is the outpouring of the hormone in the carcinoid syndrome that the cutaneous changes eventually become irreversible, constant and generalised. The patient looks polycythaemic and extremely plethoric because of a permanent hyperaemia of the face and neck with distended veins and profuse telangiectases.

Branwood and Bain[29] suggest that the cyanosis may be explained on the basis of the associated pulmonary stenosis, and the telangiectasis on liver dysfunction; but the chronic, severe and alarming colour changes seen in the carcinoid syndrome are more than can be accounted for by cardiac decompensation. They are more likely to be caused by stasis of blood in the cutaneous venules with accumulation of reduced haemoglobin in the skin. The vasoconstrictor effect of 5-HT causes increased tone of afferent arterioles, so that venous blood stagnates in the venules. The sudden appearance of bright red patches indicates that arterial blood is once again filling the capillaries.[34]

A pellagrinous type of dermatosis has been noted by Waldenström and Ljungberg.[34] The lesions may look more pruriginous and less pigmented than those of true pellagra, but diarrhoea, glossitis, mental torpor and the typical pigmentation and scaling of exposed parts may be found. It should be remembered that diarrhoea and mental changes are features of both pellagra and carcinoidosis. The pellagra may be a manifestation of a state of malnutrition resulting from the diarrhoea of the carcinoid syndrome, but it is more likely to be due to complex chemical processes. According to Page,[33] tryptophan is probably the parent substance of most of the naturally occurring indole derivatives. It is either converted to kynurenic acid, which is further metabolised to nicotinic acid, or it may take another pathway and become 5-hydroxytryptophan. Sapeika suggests that, in the carcinoid syndrome, all the available tryptophan is converted into 5-hydroxytryptamine and none is left for conversion into nicotinic acid; the lack of the precursor of nicotinic acid thus leads to the development of pellagra.

Carcinoid metastases in the skin and subcutaneous tissues are very rarely seen. I have traced only 3 cases recorded in the literature and have recently seen a fourth which is shortly to be published by Krikler, Lackner and Sealy.[47] Willis[8] reported two cases, one with a metastasis in the subcutaneous tissue and the other with a secondary deposit in the skin itself. A patient described by Bleehen[48] had several subcutaneous nodules on the front of the chest and the histology of two of them showed carcinomatous cells containing characteristic argentaffin granules. Krikler's patient, a middle-aged woman with a permanent cyanotic flush and extensive hepatic metastases, had a dull red, painless nodule, the size of a walnut, in the skin of her right shoulder; histologically this nodule consisted of a mass of argentaffin cells.

Palmar and plantar erythema in a patient with metastasising argentaffinoma has been recorded by Kierland[21] and may be due to liver dysfunction. The same patient also had *neurodermatitis* and *vitiligo*. Waldenström, Pernow and Silwer noted vitiligo in their female patient with the histamine type of flushing; she, however, did not have a carcinoid syndrome.

Lastly, MacDonald[16] remarked on the presence of *acropachyderma and pachyperiostitis* in one of the 356 cases of carcinoid which he analysed. This condition was described by Touraine, Solente and Golé (cited by Brugsch)[49] under the name of 'pachydermie plicaturée avec pachyperiostose des extrémités'; it is a systemic overgrowth of bones and skin which may be caused by abnormalities of certain endocrine glands, usually the anterior lobe of the pituitary or the gonads. It is of interest to note that malignant argentaffinoma is now regarded as a functioning endocrine tumour.

SUMMARY

The literature on the subject of malignant argentaffinoma is reviewed and the attention of dermatologists is drawn to the spectacular and unique vasomotor phenomena which are the most striking presenting features of the carcinoid syndrome.

The origin and the known physiological and pharmacological effects of the hormone, 5-hydroxytryptamine, are described with special emphasis on the present theories about the mechanisms producing the flushing and the pellagrinous dermatoses. The carcinoid flush is contrasted with that occasionally produced by histamine in the mastocytoses.

Three recorded cases of malignant argentaffinoma with cutaneous metastases are quoted and mention is made of a fourth case seen by the author in Cape Town.

Finally, other alterations of the skin that have been seen in patients with malignant argentaffinoma are enumerated.

REFERENCES

1. Biörck, G.; Axén, O. and Thorson, Å. (1952): Amer. Heart J., 44, 143.

2. Thorson, Å., Biörck, G., Biörkman, G. and Waldenström, J. (1954): *Ibid.*, **47,** 795.
3. Isler, P. and Hedinger, C. (1953): Schweiz. med. Wschr., **83,** 4.
4. Rosenbaum, F. F., Santer, D. G. and Claudon, D. B. (1953): J. Lab. Clin. Med., **42,** 941.
5. Bean, W. B., Olch, D. and Weinberg, H. B. (1955): Circulation, **12,** 1.
6. Leading Article (1955): Lancet, **2,** 1020.
7. Stacey, R. S. (1957): Proc. Roy. Soc. Med., **50,** 40.
8. Willis, R. A. (1953): *Pathology of Tumours*, 2nd ed. Butterworth: London.
9. Goble, A. J., Hay, D. R. and Sandler, M. (1955): Lancet, **2,** 1016.
10. Hudson, R. E. B. (1957): Proc. Roy. Soc. Med., **50,** 37.
11. Fraser, I. (1955): Lancet, **2,** 174.
12. Page, I. H., Corcoran, A. C., Udenfriend, S., Sjoerdsma, A. and Weissbach, H. (1955): Lancet, **1,** 198.
13. Jenkins, J. S. and Butcher, P. J. A. (1955): Lancet, **1,** 331.
14. Woolley, D. W. and Shaw, E. (1954): Brit. Med. J., **2,** 122.
15. Sapeika, N. (1956): S. Afr. Med. J., **30,** 811.
16. Macdonald, R. A. (1956): Amer. Heart J., **21,** 867.
17. Brodie, B. B., Pletscher, A. and Shore, P. A. (1955): Science, **122,** 968.
18. Rapport, M. M., Green, A. A. and Page, J. H. (1948): J. Biol. Chem, **174,** 735.
19. Erspamer, V. (1954): Pharmac. Rev., **6,** 425.
20. Lembeck, F. (1953): Nature, **172,** 910.
21. Kierland, R. R. (1957): Arch. Derm., **75,** 769.
22. Annotation (1954): Lancet, **2,** 372.
23. Pernow, B. and Waldenström, J. (1954): Lancet, **2,** 951.
24. Sjoerdsma, A., Weissbach, H. and Udenfriend, S. (1955): J. Amer. Med. Assoc., **159,** 397.
25. Snow, P. J. D., Lennard-Jones, J. E., Curzon, G. and Stacey, R. S. (1955): Lancet, **2,** 1004.
26. Jepson, J. B. (1955): Lancet, **2,** 1009.
27. Waldenström, J., Pernow, B. and Silwer, H. (1956): Acta. Med. Scand., **156,** 73.
28. Hanson, A. and Serin, F. (1955): Lancet, **2,** 1359.
29. Branwood, A. W. and Bain, A. D. (1954): *Ibid.*, **2,** 1259.
30. Barter, R. and Pearse, A. G. E. (1953): Nature, **172,** 810.
31. Feldberg, W. and Smith, A. N. (1953): Brit. J. Pharmac., **8,** 406.
32. Daugherty, G. W., Manger, W. M., Roth, G. M., Flock, E. V., Childs, D. S. Jr. and Waugh, J. M. (1955): Proc. Staff Meet. Mayo Clin., **30,** 595.
33. Page, I. H. (1954): Physiol. Rev., **34,** 563.
34. Waldenström, J. and Ljungberg, E. (1955): Acta Med. Scand., **152,** 293 and 311.
35. Bhattacharya, B. K. and Lewis, G. P. (1956): Brit. J. Pharmac., **11,** 202.
36. *Idem* (1956): *Ibid.*, **11,** 411.
37. Riley, J. F. and West, G. B. (1952): J. Physiol., **117,** 72P.
38. Riley, J. F. (1953): J. Path. Bact., **65,** 471.
39. Urbach, F. (1955): J. Invest. Derm., **25,** 211.
40. Leading Article (1956): S. Afr. Med. J., **30,** 607.
41. Rowley, D. A. and Benditt, E. P. (1956): J. Exper. Med., **103,** 399.
42. Leading Article (1956): Brit. Med. J., **2,** 219.
43. Drennan, J. M. and Beare, J. M. (1954): J. Path. Bact., **68 no. 2,** 345.
44. Montagna, W. (1956): *The Structure and Function of Skin.* New York: Academic Press Inc.
45. Marshall, J., Walker, J., Lurie, H. I., Hansen, J. D. L. and Mackenzie, D. (1957): S.Afr. Med. J., **31,** 867.
46. Becker, B. J. P. (1956): S. Afr. Practitioner, **1,** 231.
47. Krikler, D. M., Lackner, H. and Sealy, R. (1957): In the Press.
48. Bleehen, N. M. (1955): Lancet, **2,** 1362.
49. Brugsch, H. G. (1941): Arch. Intern. Med., **68,** 687.
50. Roddie, I. C., Shepherd, J. T. and Whelan, R. F. (1955): Brit. J. Pharmac., **10,** 445.

THE TUBERCULOSIS PROBLEM IN SOUTH AFRICA IN THE LIGHT OF RECENT ADVANCES*

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I deem it an honour to have been asked to introduce a line of thought for discussion at this Conference on Tuberculosis. I am glad of the opportunity for two reasons:

1. It has been my privilege to be present at two previous conferences called by the Secretary for Health, Dr. J. J. du Pré le Roux, to discuss this important national problem, namely the conference held in Durban in 1952 and the one held in Cape Town in 1955. At both these conferences we felt that we were invited at a high level to cooperate in all earnestness in coming to grips with this public health 'enemy number one' and that the Union Health Department would do all in its power to initiate and implement an effective campaign and to wage a continuous war against this enemy.

2. I have a conviction, which I feel sure must be shared by many of us, that we have reached the stage when we are in a position to group ourselves to plan our El Alamein, and may look forward with hope and enthusiasm to driving back the enemy and, within the foreseeable future, to bringing this enemy under control. With this in view I shall try to direct our thoughts along certain channels in the expectation that we shall all put our experience into the common pool so that we can plan a short-term (5 years) campaign, streamlined, and with proper emphasis where required, which can be adapted to the needs of our multi-racial population and our differing environments.

The terms 'short-term', 'multi-racial population', and 'differing environments' are deliberately used.

In any general plan for combating tuberculosis two factors are always prominent, namely (1) housing and overcrowding and (2) undernourishment. But whilst these factors are very important and are not to be overlooked, they must be regarded as belonging to a long-term policy, over which we have limited control and which cannot be considered in any *short-term campaign.*

Multi-racial population: We must not forget that we will have to adapt our policies to the 4 racial groups and their ways of life—Europeans, Coloured, Natives and Indians.

Differing environments: We must be prepared to realize that the tuberculosis problem presents itself in a somewhat different way in rural areas as compared with densely populated urban areas. Again the importance of the problem of tuberculosis is relatively different in centres like Cape Town, Port Elizabeth, East London, Durban and Maritzburg from the problem in Johannesburg, Pretoria and Bloemfontein; and, again, different from that in the areas and centres in the Native territories.

THE CHANGED POSITION

Let us now take stock of the position and see to what extent we are in a better position to cope with the situation than we were say 40 years ago, and assess the useful lessons we have learnt since that time. Until then we in this country were groping our way with worthy stubbornness and doing our unflagging best against odds which often dismayed and disheartened us but never reduced us to despair or caused us to lose our faith that in the future the state of siege would be lifted and that we should go on to the attack in a conquering way.

Until about 40 years ago, the tuberculosis spectre was well described by Sir William Osler as 'the captain of the men of death who stalks the land relentlessly claiming its 8 or 9 or 10% of all deaths, day in, day out, all the time'. This was the time when stigma, superstition and despair were often uppermost in

* Introductory address, Tuberculosis Conference, Johannesburg, 2-4 December 1957.

the minds of those who were confronted with tuberculosis in themselves and their relatives or friends. The result was that most people were prepared to evade detection of the disease until it could not be hidden any longer. All this imparted to tuberculosis a fear, a hush-hush attitude and a sense of inevitableness which, though not unnatural, made it a public-health problem of even greater magnitude than it really was—and that was big enough—because of the frustrations which beset every effort to cure and prevent this deadly disease.

Recognition, both by the doctor and the family, was often late, delayed until the disease had reached an advanced stage when the hope of recovery could not be put forward with any confidence except among the privileged classes who could afford to arrange for a prolonged rest cure in one of the few sanatoriums then available in different parts of the world. Besides the cost involved, it required patience, courage and faith on the part of the patient to submit to the lengthy course of treatment then prescribed to assist nature to bring about a cure.

A seemingly hopeless position existed and the lack of beds meant long waiting lists of cases becoming more and more advanced with every month that passed, with the result that the majority of cases untimately admitted came to hospital but to die.

We were well and truly in the doldrums at this stage of our campaign against tuberculosis and there was very little we could do to break the vicious circle—the spread of the infection giving rise to fresh cases, which became advanced cases because the only available means of cure was long retention in hospital and sanatorium beds, which were not available. This led to the abandonment of hope of a cure on the part of the lesser privileged—especially the non-Europeans—and reluctance to go to hospital to die away from home; and so again the start of a new spread of infection in overcrowded homes.

But enough of this morbid story! It does serve a purpose in so far that we should not forget the pioneering efforts of the Union Health Department (here I should like to mention the name of Dr. J. A. Mitchell) and of some of our senior local authorities (here I should like to mention Dr. Jasper Anderson and Dr. Charles Porter).

'*The old order changeth yielding place to new.*' The first signs of a significant change in our attitude and approach, and in our determination to deal with this almost overwhelming problem of tuberculosis, became apparent after the First World War. Overseas, public opinion swung in favour of a better and more secure welfare state for everybody, and found an echo in our country. Another stimulus may well have been the influenza pandemic of 1918-19, which certainly hastened our Public Health Act 36 of 1919.

So we entered *the second phase* of our fight against tuberculosis. Local authorities were encouraged by the financial assistance made available by the Union Health Department, and hospital and sanatorium beds were provided on a greater scale than before; clinical services were extended through subsidized clinics in all the larger local-authority areas; health visitors and clinic sisters were appointed to enter the field of preventive medicine.

At this stage we can list the various protective bulwarks which we considered necessary to use in our attempt to protect ourselves against tuberculosis:

1. Notification and statistics; to get to know the extent of the problem.
2. An enlightened public.
3. Better housing; to prevent overcrowding and mass infection.
4. Better nutrition; to combat under-nourishment amongst large sections of the community.
5. Hospitals and sanatoriums for treatment.
6. Clinics for detection and treatment.
7. Protection of foodstuffs, particularly pasteurization of milk against bovine tuberculosis.
8. Rehabilitation; to bring the cured back to citizenship.

It is not an easy matter to bring all these defence elements into a comprehensive scheme which will give the best results in each area, and we shall differ amongst ourselves on the relative importance and emphasis to be placed on some of these defensive measures.

NEW WEAPONS

We now have to concentrate on *the third phase*, based on new weapons we have at our disposal; the future success of our short-term campaign will depend on how boldly we use these new weapons in supplementing or replacing the old weapons we have had to use until now. The new weapons are 4 in number, as follows:

1. New therapeutic antibiotics and other drugs, e.g. streptomycin, INH and PAS.
2. SANTA settlements and aid to dependants.
3. BCG vaccine and mass radiography.
4. Government support and aid; invalidity grants and child welfare grants.

Let us briefly examine the possibilities of these 4 weapons in order to determine what role they can play in a short-term plan in our campaign against tuberculosis.

New Therapeutic Antibiotics and Drugs

Speaking generally we can accept that there is a definite place for this new weapon in

(*a*) a quicker cure for tuberculosis, whether the treatment is undertaken in hospital or sanatorium, or in ambulatory treatment at clinics or in domiciliary treatment; and

(*b*) the use of this treatment in converting 'positive' cases (TB in the sputum) into 'negative' cases (TB-free sputum) thus contributing to the solution of the problem presented by the presence of infectious cases in the household or community.

This weapon can be brought into immediate use in hospital, if a bed is available; in domiciliary and ambulatory cases before hospitalization, if a bed is not available; or in continuation treatment after hospitalization.

SANTA Settlements and Aid to Dependents

(*a*) *Settlements.* Before commenting upon these two SANTA projects, I should like to express my conviction that the National Tuberculosis Fund inaugurated during the Van Riebeeck tercentenary celebrations, stimulated the public in the Union of South Africa as never before, and the tuberculosis-mindedness of our people today can, directly and indirectly, be placed in an appreciable measure to the credit of that national fund-raising effort. The SANTA settlement scheme is a project that will play an important part in the campaign against tuberculosis as an auxiliary adjunct to sanatoriums and hospitals. Whether it will play the same useful part in large local-authority areas with substantial tuberculosis hospitals and sanatoriums that it can and will play in the areas of smaller local authorities remains to be seen.

The expansion of the settlement service could advantageously be undertaken in the rural areas and the areas of small local authorities as a pre-hospital service and a post-hospital adjunct.

I take this opportunity of stressing the importance of adequate bed accommodation for tuberculosis patients, and of urging that sanatoriums, hospitals and settlements should be taken together in working out the solution of this phase of our problem.

(*b*) *Aid to Dependants.* In this respect a service is being rendered which fills a hiatus that cannot be adequately closed in any other way. It stimulates continued public interest in voluntary effort and helps to keep together the family in which the tuberculosis patient is notified, whilst encouraging the patient to seek early treatment in an institution or otherwise.

BCG Vaccination and Mass X-ray

Here our immediate objective should be

(*a*) to confer protective resistance on all the medical students and nursing staffs in all our hospitals who are found to give a negative reaction to the tuberculin skin test.

(*b*) to ensure that all children, where reasonably possible, are provided with that protection before they leave school. To achieve this, it will be necessary to institute a two-fold approach; the one aiming at conferring protection on the infants born in those communities where the danger of infection is greatest, as soon after birth as possible; the other by offering BCG vaccination to all established negative reactors.

The experience and conclusions of those who have undertaken extensive work in this field have been that a negative X-ray report without a tuberculin test may give a false sense of security, and that a positive tuberculin test without radiography is incomplete.

A reasonable practical approach would thus be to have all three procedures at hand and available for use. The routine examination would be as follows:

1. The tuberculin skin test.

2. All those who show definite negative reactions to be offered BCG vaccination.
3. All those who show definite positive reactions to be X-rayed to determine whether there is any active lesion which requires further investigation and treatment.

Mass X-ray facilities have a special public-opinion appeal. Whilst it is true that with the advent of the new therapeutic agencies we are far better equipped to deal with many more cases much more expeditiously, we should nevertheless only undertake this intensive search for every early case in communities where it will be possible to place these cases under adequate treatment straight away. Only in this way shall we avoid disappointments and loss of faith on the part of the public.

Government Support and Aid

The need for assistance from the Government is now well established, and all that is required is to ensure that the grants which the Government makes come through with the least possible delay. It is hoped also that these grants may in time be increased to ensure as nearly as possible the normal standard of living of the household during the time that the patient is undergoing treatment and being cured of the disease.

The fact that tuberculosis acquired in certain services qualifies for recognition under the Workmen's Compensation Act is a step in the right direction and should be extended.

Conclusion

To sum up, let our aim be

1. *In our treatment*

to convert hopeful assistance to nature in overcoming the disease into active treatment, and thus to force a cure.

2. *In our preventive measures*

let us get beyond the stage of relying on complete isolation, or the dilution of the infection where such isolation is not possible. Let us now undertake active preventive measures by converting our positive-sputum cases into negative-sputum cases, and vaccinating our newborn children to give them an early resistance to the disease.

In other words—plan to attack rather than plan to defend.

BCG Vaccination and Tuberculin Testing in the Cape Divisional Council Area

When in 1949 the Council first recruited non-European nurse aids for the Dr. A. J. Stals Memorial Sanatorium, it was decided to tuberculin-test all the trainees, and those who were non-reactors were given BCG vaccine in an attempt to protect them from the infection to which they would inevitably be exposed. BCG was specially imported for this purpose from the Statums Serum Institute in Copenhagen. Successive batches of nurse aids have been tuberculin tested and all non-reactors have been similarly vaccinated. All but one of these girls (a total of 44) have converted to tuberculin-positive and none of them has developed pulmonary tuberculosis at the Sanatorium.

For some years past I have been convinced that BCG should be used as one line of attack in our campaign in South Africa against tuberculosis, and at the Durban Tuberculosis Conference (1952) I agreed that the Divisional Council Health Department would undertake a pilot BCG scheme. For various reasons little progress was made until a small supply of Glaxo freeze-dried BCG vaccine became available this year.

Since that time 187 children have been given freeze-dried BCG vaccine and it is hoped to expand our programme considerably as soon as further supplies become available. In no case have any untoward reactions followed the use of this freeze-dried vaccine. To date 104 of these vaccinated children have returned for tuberculin testing after 6 weeks or more, and of these only 4 are still tuberculin-negative. The children chosen for this small experiment have been tuberculin-negative contacts of open tuberculosis cases—14 of them European and the balance Cape Coloured. No special measures have been taken to isolate the vaccinated children from the source of infection, although in a number of cases the patient was, in fact, removed to hospital before the vaccination was offered. The experiment is promising but of course no conclusions can be drawn at this early stage.

The 'Heaf test', using Heaf's multiple puncture apparatus and Allen and Hanbury's 'protoderm' concentrated tuberculin PPD, has been used largely in detecting the non-reactors among contact children and in performing the post-vaccination tuberculin testing. Dr. Mitchell, the Council's Deputy Medical Officer of Health, saw this apparatus in use when he visited the Northern Ireland Tuberculosis Authority during his WHO Fellowship last year and was much impressed with its possibilities for mass tuberculin testing. The apparatus itself costs about £9 and the protoderm retails in Cape Town at 6s. 2d. per millilitre. With this apparatus, it has been found possible to perform 400 tests in an hour, using only 1 ml. of tuberculin PPD. The test is very easy to perform, is completely painless, and is not resented by children. Another advantage is that the test is unaffected by varying techniques of different operators and can readily be performed by health visitors or anyone else with a bit of common sense who has been shown how to do it. The reading of this test is simplicity itself and the degree of positivity leave little room for variation between different observers. A further great advantage is that positive results persist much longer than a positive 'Mantoux' and are easily readable after a lapse of 7 days. This means that children who have been tested at a clinic session can be asked to report to the next session on the same day the following week. Administration is therefore simplified and the defaulter rate much reduced. When to these facts is added the low cost per test and the fact that the protoderm appears to remain potent indefinitely, I have no hesitation in recommending the Heaf test to anybody doing tuberculin testing on a large scale.

Tuberculosis in Cape Division
(excluding Cape Town and Simonstown Municipalities)

PULMONARY TUBERCULOSIS

Year	Notifications			Deaths		
	Eur.	*non-Eur.*	*Total*	*Eur.*	*non-Eur.*	*Total*
1940	65	479	544	22	220	242
1945	48	498	546	7	124	131
1950	134	943	1,077	31	223	254
1956	103	1,263	1,366	8	105	113

TUBERCULOSIS MENINGITIS

1956	4	62	66	1	28	29

TUBERCULOSIS: HOSPITAL ADMISSIONS

Year	*Eur.*	*non-Eur.*	*Total*
1940	34	72	106
1945	34	87	121
1950	85	61	146
1954	115	239	354

TUBERCULOSIS PATIENTS IN HOSPITAL, 11 OCTOBER 1957

European		*non-European*		*Total*
Male	*Female*	*Male*	*Female*	
30	20	243	157	450

TUBERCULOSIS: AMBULATORY AND DOMICILIARY TREATMENT

	Eur.	*non-Eur.*	*Total*
February 1956	54	531	585
August 1956	27	555	582
February 1957	49	714	763
August 1957	42	588	630

FULL-SIZE X-RAYS

Year ended 31 July 1957, 2,400.

SPECIAL TUBERCULOSIS CLINIC SESSIONS

	Eur.	*non-Eur.*	*Total*
Clinic sessions per week ..	3	8	11
Total attendance per week ..	—	—	550
Total attendance per session per week	25	59	—

ADDENDUM

TUBERCULOSIS: A DISCUSSION ON THE MERITS OF AMBULATORY TREATMENT AS COMPARED WITH INSTITUTIONAL TREATMENT

In consultation with some of our medical officers, particularly Dr. R. L. Tobias, our Physician-Specialist, we consider that the following points are worth stressing in assessing thesi potion.

We all agree that hospitalization is the ideal in most cases, and should not be replaced by ambulatory or domiciliary treatment. The following points, however indicate the role that ambulatory and domiciliary treatment can play in the general campaign:

1. Since we have instituted ambulatory and domiciliary treatment, we have been impressed by the increasing confidence and cooperation shown by the patients, particularly non-Europeans. This has developed from the knowledge that, while awaiting hospitalization, they are at least receiving treatment which makes an impression on the disease, rather than the cod liver oil cough mixture regime used previously.

2. *Pre-hospital treatment* often renders the sputum negative within a comparatively short time, and thus lessens the danger to *contacts*. This fact is particularly important when our long non-European waiting lists are borne in mind.

3. *Post-hospital treatment*, which permits *earlier discharge* from hospital and, often, *return to work* (where arrangements can be made for time off to visit the clinic two or three times a week for injections), ensures a closer supervision in cases which are healing but not entirely quiescent.

4. The treatment of children, particularly where one can combine antibiotics with a feeding scheme—as for instance in conjunction with our baby clinics—is often very successful. Primary complexes in older children, in our opinion, are often not cases for prolonged hospital treatment. It is psychologically bad for children to be separated from their families for any length of time. The difficulties often encountered in returning non-European children to their homes after prolonged therapy, where the families are uninterested or have left the area, are a problem to hospital authorities. Ambulatory and domiciliary treatment of this type of child is very effective and compares favourably with hospital treatment, except in the very young and the very ill.

5. For patients who refuse hospital treatment, one now has medicines with which some treatment—often successful—can be given. These patients previously had no treatment whatsoever, and were difficult to control.

6. Finally there is a group, particularly amongst the mass-survey cases, where a small lesion exists which is either early tuberculosis (which will usually clear well with ambulatory treatment even while the patient is at work) or where the diagnosis despite investigation cannot be confirmed and a course of treatment as a therapeutic test is of use. These patients are obviously unsuitable for prolonged and expensive hospitalization. Despite propaganda, there is still unfortunately a stigma attaching to a diagnosis of tuberculosis. This fact, together with the obvious risk of infection in a general ward with open cases, makes the admission of such 'observation' cases highly undesirable, unless there are special indications for it.

ASSOCIATION'S BRONZE MEDAL

The following citations were read at the adjourned annual general meeting of the Medical Association of South Africa held at Durban on 16 September 1957, when the Association's bronze medals for meritorious service were presented to the undermentioned members:

MR. B. A. ARMITAGE

Mr. Bernard Albert Armitage was born in Pietermaritzburg and received his early education at Maritzburg College. He then proceeded to Edinburgh, where he qualified L.D.S. (R.C.S.) in 1930, and, continuing his medical studies, obtained the degree L.R.C.P. & S. (Edinburgh) and L.R.F.P.S. (Glasgow) in 1931.

Mr. B. A. Armitage

Returning to South Africa he practised as a medical officer for 2 years at Grey's Hospital, Pietermaritzburg In 1935 he returned to Edinburgh and became a Fellow of the Royal College of Surgeons. He then commenced general practice in Pietermaritzburg. In 1936 he was appointed a member of the Senior honorary staff as a Surgeon of Grey's Hospital, Pietermaritzburg, and holds the position of Senior Honorary Surgeon of the same Hospital at the present time. In 1951 he became a specialist surgeon and, apart from general surgery, has always pioneered the field of maxillary-aural-facial surgery in Pietermaritzburg. Mr. Armitage joined the Medical Association of South Africa in 1935, and has always been a most ardent worker for the Association. In 1936 he was Honorary Secretary of the Surgical Section of the Medical Congress held in Pietermaritzburg, and from 1937 to 1941 he was Honorary Secretary of the Natal Inland Branch, a position which he held again in 1945. In 1942 the Branch elected him as its President for that year. He has been a member of Federal Council since 1945. Since his election to Federal Council he has served on the Central Committee for Contract Practice and has been the guiding star of the Branch in matters of contract practice and work of a medico-political type, on which subjects he is most interested and well informed. During the last World War, on being found medically unfit for service, Mr. Armitage was elected Secretary of the Local Emergency Committee, giving of his best, as usual, and spending a great deal of time and effort in the service of this committee. In 1953 Mr. Armitage was elected as the representative of the Natal Inland Branch on the Joint Standing Advisory Council of the University of Natal and the Natal Provincial Administration, in which capacity he is still serving. To the work of this Council he has also given much energy and a considerable amount of his valuable time. He was appointed a member of the Visiting Staff of Edendale non-European Hospital, when it was opened in 1954. Outside of his professional duties he has been a member of Rotary since 1936 and is a Past President. He has also contributed greatly to the work of the South African Red Cross since 1939, having held the offices of Chairman and Vice-Chairman of the Local Committee, and is now a Life Member. In recognition of his loyal and devoted service to his profession and his untiring work for the Medical Association of South Africa, the Association is pleased to award to Mr. Armitage its Bronze Medal for meritorious service.

DR. AARON BROOMBERG

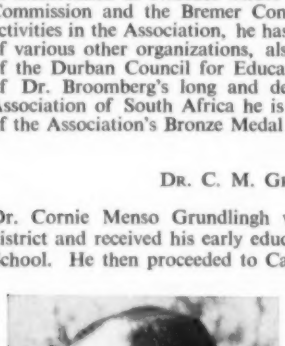
Dr. Aaron Broomberg was born at St. James, Cape Town, and educated at the Commercial High School, Johannesburg, from where he matriculated in 1920. He graduated as Bachelor of Medicine and Bachelor of Surgery at the University of the Witwatersrand in 1927 and commenced practice in Natal in 1928.

Dr. A. Broomberg

Since 1930 he has been in general practice in Durban. In 1945 he was elected to the Council of the Natal Coastal Branch, on which he has served continuously to date. In 1946 he was the Organizing Secretary of the first post-War South African Medical Congress, which took place in Durban. He acted as Secretary of his Branch from 1947 to 1949 and was elected as its President for 1951. During 1956 and 1957 he was Chairman of the Organizing Committee of the 41st Medical Congress which was held in Durban in September 1957. He has been a member of the Federal Council since 1947 and has served on its Central Ethical Committee and the Central Committee for Contract Practice. Dr. Broomberg also served his Branch on numerous Committees, in many instances as Chairman, such as his Chairmanship in 1954-55 of the Committee for investigation of Factory and Industrial Medical Practice and in 1956 of the Committee for investigation of the Integration of General Practitioners into Provincial Hospital Services. He did a great deal towards the establishment of the Medical Faculty of the University of Natal and has assisted in building up the Medical Library of the University. He was a Branch nominee during 1953-55 of the Provincial Hospital Advisory Council and was a member of the Committee responsible for the preparation of memoranda as evidence before the Natal Hospitals Advisory Commission and the Bremer Commission. In addition to his activities in the Association, he has been a member of committees of various other organizations, also acting as Chairman in 1957 of the Durban Council for Education on Alcoholism. In view of Dr. Broomberg's long and devoted service to the Medical Association of South Africa he is to be honoured by the award of the Association's Bronze Medal for meritorious service.

Dr. C. M. Grundlingh

Dr. Cornie Menso Grundlingh was born in the Ventersdorp district and received his early education at the Ventersdorp High School. He then proceeded to Cape Town University, where he graduated as Bachelor of Medicine and Bachelor of Surgery in 1936. He commenced general practice in Pretoria in 1938 and during the same year became a member of the Medical Association of South Africa. During the last World War he joined the South African Medical Corps, and was on active service abroad. From the very inception Dr. Grundlingh has displayed a very keen interest in the affairs of the Medical Association. He has served on the Branch Council of the Northern Transvaal Branch continuously since 1946 except during the period 1952-54, when ill health forced him to relinquish office. He acted as Honorary Secretary of the Branch from 1947 to 1949, and in 1950 the Branch saw fit to honour him by electing him as its President for that year. He held this post with distinction and steered the Branch successfully through a difficult period. Dr. Grundlingh is a member of the Federal Council of the Association. Dr. Grundlingh was the Organizing Secretary of the South African Medical Congress held in Pretoria in 1948. His outstanding ability and the success which crowned his efforts were recognized so that, although dogged by ill-health over a period, he was prevailed upon to accept the office of Joint Organizing Secretary of the 1955 Congress which took place in that city. Once again he did not spare himself in contributing to the success of that Congress. In addition to his devoted service to the Association, Dr. Grundlingh has continued to serve his country in recent years as Commanding Officer of a Field Ambulance Unit. His loyal and distinguished long service in the Active Citizen Force has been recognized by the award of the John Chard Medal. The Association wishes to honour him for his work on its behalf by the award of its Bronze Medal for meritorious service.



Dr. C. M. Grundlingh

Dr. Maurice Shapiro

Dr. Maurice Shapiro, who was born in Johannesburg and educated at the Jeppe High School, graduated as Bachelor of Medicine and Bachelor of Surgery at the University of the Witwatersrand in 1929 and has been in general practice since that time. He has taken an active part in the work of the Medical Association, having been a member of the Southern Transvaal Branch Council for some 16 years, and is a Past President of that Branch. He has been a member of Federal Council for the past 12 years and was a member of the Executive Committee of Federal Council, of the Augmented Executive Committee of the Association for the Transvaal, and Chairman of the Federal Council Committee on the Economics of Medical Practice. He is also a member of the Transvaal Hospitals Advisory Council and took a leading and distinguished part in the fight for an Ordinance which would be fair to the medical profession when it was proposed to introduce free hospitalization into the Transvaal. He is Chairman of the Tara Hospital Board and an Honorary Lecturer in the Department of Clinical Pathology of the University of the Witwatersrand. He was also associated with the establishment of the Medical Graduates Association of the University of the Witwatersrand, of which he is a Past President. Apart from his work for the Association, Dr. Shapiro was a founder member of the Rand Blood Transfusion Service, which afterwards became the South African Blood Transfusion Service, and has been its part-time Medical Director for the past 10 years, although he has been in charge of its technical services almost since its inception. He is a member of the Editorial Board of *Vox Sanquinis*, the official journal of the International Society of Blood Transfusion, and was elected a member of the International Bureau of this Society in 1953. Dr. Shapiro has made distinguished contributions in the field of blood-group research and was awarded the Hamilton Maynard Memorial Medal of the Medical Association as the author of the most outstanding paper published in the *South African Medical Journal* in 1951. He has been a member of the South African Medical and Dental Council for the last 8 years. Dr. Shapiro has been enthusiastic and tireless in his work for the Association and the profession, particularly in the Transvaal, and the Association wishes to show its appreciation by bestowing on him the honour of the award of the Association's Bronze Medal for meritorious service.

Dr. M. Shapiro

DR. RAYMUND THERON

Dr. Raymund Theron is gebore te Murraysburg, K.P., en het sy skoolopleiding by verskillende skole gehad. In 1908 het hy aan die Jongens Hoërskool, Stellenbosch, gematrikuleer, waarna hy aan die Victoria Kollege, Stellenbosch, die B.A. graad verwerf het. Hy is toe na Londen waar hy aan die *London Hospital* gestudeer het en in 1917 die grade M.R.C.S. en L.R.C.P. behaal het. Na militêre diens tydens die Eerste Wêreldoorlog het hy na die *London Hospital* teruggekeer en in 1919 die grade M.B., B.S. en in 1921 die graad M.D. in verloskunde en ginekologie verwerf. Na verdere studie, o.a. ook aan die Kermaurnerkliniek te Weenen, het hy in 1923 na Suid-Afrika teruggekeer en in Bloemfontein as algemene praktisyn begin praktiseer. In die Tweede Wêreldoorlog het dr. Theron diens gedoen as Bevelvoerende Offisier van 'n Ongevalle - Opruimingshospitaal in Oos-Afrika, en daarna van 'n hospitaal vir herstellende gevalle in Egipte. Hiervoor is hy tweemaal met eervolle vermelding in verslae genoem. Na verdere diens op Ermelo is hy in 1943 terug na sy praktyk in Bloemfontein, waar hy hom nou toegelê het op verloskunde en ginekologie en in 1945 sy naam op die register van spesialiste laat plaas het. Reeds as student was hy lid van die Britse Mediese Vereniging en by sy terugkeer na Suid-Afrika het hy lid geword van die Tak O.V.S. en Basoetoland van daardie Vereniging, wat later oorgegaan het as 'n tak van die Mediese Vereniging van Suid-Afrika. Van die begin af was hy 'n aktiewe lid van die Vereniging. Hy is 'n bestuurslid van die tak, het gedien as Tesourier en was tweemaal Voorsitter en wel in 1939 en weer in 1944. In 1945 is hy gekies as verteenwoordiger van sy tak op die Federale Raad en van daardie jaar af dien hy op die Uitvoerende Komitee van die Raad en was vir 'n aantal jare Onder-Voorsitter totdat hy as Ere-Voorsitter van die Vereniging vir die jaar 1951-52 gekies is. As lid van die Vergrote Uitvoerende Komitee van die Federale Raad het hy in die hitte van die stryd i.v.m. hospitaaldienste gedurende die afgelope 10 jaar gestaan. Dr. Theron is in 1922 met dr. Emilia Krause in Londen getroud en uit die huwelik is twee dogters en 'n seun gebore. By sy kollegas is dr. Theron in wye kringe bekend vir sy opregte kollegialiteit, sy bereidheid om andere te help en vir sy onberispelike eerlikheid en deeglikheid. Vir sy pasiënte was hy troue dokter en huisvriend en menige een het dit betreur dat hulle hom nie langer as huisdokter kon behou toe hy as spesialis geregistreer is nie. Die tyd, werk en inkomste wat dr. Theron opgeoffer het deur sy deelname aan die werksaamhede van die Mediese Vereniging en ten behoewe van die geneeskundige beroep is nie te bereken nie, dog hy het nooit moeite of tyd ontsien nie. Hy was altyd te vinde as daar moeilikheid was wat op oplossing gewag het. Sy mooi persoonlikheid, sy getroue pogings en ryke gees het die verenigingslewe verryk en geïnspireer. Vir sy getroue dienste aan die Vereniging wat hy op so 'n stil en besadigde manier dog met volharding gelewer het, wil die Vereniging hom graag vereer met die toekenning van die Brons Medalje vir waardevolle diens.

Dr. R. Theron

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG: SIXTH PROFESSIONAL EXAMINATION FOR THE DEGREE OF M.B., B.Ch.

The following candidates have completed all the requirements of the Sixth Professional Examination for the degree of M.B., B.Ch.:

Bastomsky, C. H.
Bekker, D.
Berman, L.
Blecher, J. A.
Bleloch, J. A.
Booysen, E. L.
Brenner, H.
Brereton, D. N.
Brown, J. D. F.
Carr, D.
Cartwright, J. D.
Chaitowitz, A.
Christianakis, P.
Cominos, D. C.
Cope, S.
De Clerq, L. D.
de Reynier, C.-H.
Dimopoulos, G.
Duckworth, W. C.
Esmonde-White, M. F.
Gamsu, L.
Gilchrist, G. S.
Goldman, A.
Goodman, B.
Harvey, A.-M.
Hoffman, G.
Hoppenstein, R.
Ismail, H.
Kaplan, I. L.
Khan, H.
Klintworth, G. K.
Koor, A. R. I.
La Rocca, E. V.
Lowenthal, M. N.
Manga, D. B.
Mbonyana, C. P. B. K. M.
Mendelow, A. L.
Mia, I. M.
Miller, N.
Mokhobo, K. P.
Myers, D. N. M.
Nxumalo, A. M.
Obel, I. W. P.
Ordman, J. A.
Orelowitz, S. M.
Padayatchi, P.
Pearlman, T.
Perdikis, P.
Potgieter, I.
Rachmann, K. W.
Rathebe, A. L. K.
Raubenheimer, A. A.
Rayman, A.
Rivlin, M. E.
Rosenberg, M. T.
Rudick, J.
Russell, L. G.
Sarzin, B.
Sechiari, G. P.
Sirkin, L. L.
Smit, E.
Sonik, S.
Stern, B. E.
Taitz, L. S.
Toker, E.
van Straaten, Y.
Vorster, W. A. D.
Vos, H. P.
Waldman, H. L.
Weinbrenn, G. H.
Woeber, K. A.
Wulfsohn, M. A.

29 November 1957

BOOKS RECEIVED RECENTLY IN THE WITWATERSRAND MEDICAL LIBRARY

Aitken, J. T. A manual of human anatomy by J. T. Aitken and others. 1956. 5 v. Edinburgh: Livingstone.

Alvarez, Walter C. Medical writing by Walter C. Alvarez, Hugh Clegg and others. (*c* 1956). N.Y.: MD Publications.

American College of Chest Physicians. Clinical cardiopulmonary physiology, etc. N.Y. etc. Grune & Stratton. 1957. Contains bibliogrs.

American Medical Association. Council on Scientific Assembly. A.M.A. scientific exhibits 1955. N.Y.: Grune & Stratton. 1955.

Journal. J.A.M.A. clinical abstracts of diagnosis and treatment published with the approval of the Board of Trustees, American Medical Association. N.Y.: Intercontinental medical book corporation. 1957.

Arruga, H. Ocular surgery transl. from the 4th Spanish ed. by M. J. Hogan and L. E. Chaparro etc. N.Y.: etc. Mc-Graw-Hill. 1956. Contains bibliogrs.

Averill, L. A. Psychology applied to nursing by L. A. Averill and F. C. Kempf, 5 ed. etc. Philadelphia etc.: Saunders. 1956.

Baer, R. L. Allergic dermatoses due to physical agents ed. by R. L. Baer etc. Philadelphia: Lippincott (1956).

Barach, A. L. Pulmonary emphysema, ed. by A. L. Barach and H. A. Bickerman etc. Baltimore: Williams & Wilkins. 1956. Contains bibliogrs.

Barnett, Anthony. The human species: a biology of man. Harmondsworth: Penguin. 1957. (Pelican Books.) First published in 1950.

Barnett, E. de Barry. Mechanism or organic chemical reactions by E. de Barry Barnett etc. London: Blackie (1956 rep. 1957).

Barrow, D. W. The clinical management of varicose veins, 2 ed. rev. and enl. (N.Y.): Hoeber (c1957).

Beierwaltes, W. H. Clinical use of radioisotopes, by W. H. Beierwaltes, P. C. Johnson and A. J. Solari etc. Philadelphia etc.: Saunders 1957. Contains bibliogrs.

Belcher, Ronald. New methods in analytical chemistry by R. Belcher and C. L. Wilson etc. (London): Chapman & Hall (1955) rev. 1956. Contains bibliogrs.

Blaikston's New Gould medical dictionary, a modern comprehensive dictionary of the terms used in all branches of medicine and allied sciences. Editors: Normans L. Hoerr and A. Osol, 2 ed. NY. etc.: Blakiston 1956.

Bogardus, E. S. Sociology applied to nursing by E. S. Bogardus and A. B. Brethorst etc. 3 ed. Philadelphia: Saunders (c1952). Reprinted 1953.

Bray, H. G. Kinetics and thermodynamics in biochemistry by H. G. Bray and K. White etc. London: Churchill 1957. Contains bibliogrs.

Carleton, H. M. Histological technique for normal and pathological tissues and the identification of parasites by H. M. Carleton with the collaboration of R. A. B. Drury etc. 3 ed. London: O.U.P. 1957.

Charnley, John. The closed treatment of common fractures. 2 ed. Edinburgh: Livingstone. 1957.

Chayer, M. E. Nursing in modern society by M. E. Chayer etc. N.Y.: Putnam's sons (c 1947).

Clark, W. M. Topics in physical chemistry: a supplementary text for students of medicine. 2 ed. Baltimore: Williams & Wilkins. 1952. Contains bibliogr.

Commission on Chronic Illness. Chronic illness in the United States etc. Cambridge, Mass.: Published for the Commonwealth Fund by Harvard U.P. 1957. Contains bibliogrs. W.M.L. has v. 1. Prevention of chronic illness.

Coulter, P. P. The nurse in the public health program by P. P. Coulter etc. N.Y.: Putnam's sons (c 1954).

Courchaine, A. J. Chemistry visualized and applied by A. J. Courchaine, ed. by M. C. Cowan, drawings by R. Albany. N.Y.: Putnam's sons (c 1957). Contains bibliogrs.

Cumming, Elaine. Closed ranks: an experiment in mental health education by E. Cumming and J. Cumming etc. Cambridge, Mass.: Published for the Commonwealth Fund by Harvard U.P. 1957.

Dienstein, William. Technics for the crime investigator by W. Dienstein etc. Springfield: Charles Thomas. 1956.

Dobzhansky, Theodosius. The biological basis of human freedom. N.Y.: Columbia University Press. 1956.

Dorland, W. A. N. Dorland's illustrated medical dictionary. 23 ed. etc. Philadelphia etc.: Saunders. 1957. Earlier ed. entitled the American illustrated dictionary.

Fieser, L. F. Natural products related to phenanthrene by L. F. Fieser and M. Fieser. 3 ed. etc. N.Y.: Reinhold. 1949. (Monograph series no. 70.) (American Chemical Soc.) Previously entitled 'Chemistry of natural products related to phenanthrene' by L. F. Fieser.

Finer, Herman. Administration and the nursing services etc. N.Y.: Macmillan. (1952 repr. 1955.)

Fishbein, Morris. The handy home medical adviser and concise medical encyclopedia etc. N.Y.: Hanover house (c 1957).

Foster, J. W. Chemical activities of fungi etc. N.Y.: Academic press. 1949.

Francis, G. E. Isotopic tracers: a theoretical and practical manual for biological students and research workers by G. E. Francis, W. Mulligan and A. Wormall etc. London: Athlone press. 1954. Contains bibliogrs.

Gardner, Martin. Mathematics magic and mystery. N.Y.: Dover publications (c 1956).

Gilman, Henry. Organic chemistry: an advanced treatise etc. N.Y.: John Wiley. 1943-1953. 4 v.

Greenberg, D. M. Chemical pathways of metabolism etc. N.Y.: Academic press. 1954. 2 v.

Haagensen, C. D. Diseases of the breast by C. D. Haagensen etc. Philadelphia etc.: Saunders. 1956. Contains bibliogrs.

Hallowell, A. I. Culture and experience. Philadelphia: University of Pennsylvania. 1955.

Harrison, G. A. Chemical methods in clinical medicine, their application and interpretation with techniques of simple tests. 4 ed. etc. London: Churchill. 1957. Contains bibliogrs.

Heidelberger, Michael. Lectures in immunochemistry etc. N.Y.: Academic press. 1956. Contains bibliogrs.

Heidgerken, Loretta. Principles of learning and teaching: a study guide for educational psychology by L. Heidgerken etc. Philadelphia: Lippincott (c 1956). Contains bibliogrs. Mimeographed.

Henry, A. K. Extensile exposure by A. K. Henry. 2 ed. Edinburgh etc.: Livingstone. 1957.

Hoagland, Hudson, ed. Hormones, brain function and behaviour: proceedings of a conference on Neuroendocrinology held at Arden House, Harriman, New York, 1956 etc. N.Y.: Academic press. 1957. Contains bibliogrs.

Hunt, A. M. Anesthesia: principles and practices, a presentation for the nursing profession. N.Y.: Putnam's sons (c 1948).

Johnson, F. H., ed. The luminescence of biological systems: proceedings of the Conference on Luminescence March 28-April 2, 1954, sponsored by the Committee on Photobiology of the National Academy of Sciences—National Research Council and supported by the National Science Foundation. Washington: American Ass. Advancement of Science. 1955. Contains bibliogrs.

Ingraham, F. D. Neurosurgery of infancy and childhood by F. D. Ingraham and D. D. Matson etc. Springfield, Illinois: Charles C. Thomas (c 1954).

Klotz, I. M. Some principles of energetics in biochemical reactions etc. N.Y.: Academic press. 1957.

Lederer, Edgar. Chromatography: a review of principles and applications by E. Lederer and M. Lederer. 2 ed. rev. and enl. Amsterdam, London etc.: Elsevier. 1957.

Long, E. R. A history of the therapy of tuberculosis and the case of Frederic Chopin etc. Lawrence: University of Kansas. 1956. (Logan Clendening Lectures on the history and philosophy of medicine. 6th series.)

Lowsley, O. S. Clinical urology by O. S. Lowsley and T. J. Kirwin, drawings by W. P. Didusch. 3 ed. Baltimore: Williams & Wilkins. 1956. 2 v. Contains bibliogrs.

Lubs, H. A., ed. The chemistry of synthetic dyes and pigments, ed. by H. A. Lubs etc. N.Y.: Reinhold publishing co. 1955. Contains bibliogrs. (American Chemical Society. Monograph 127.)

McAllister, J. B. Ethics with special application to the medical and nursing professions. 2 ed. Philadelphia etc.: Saunders. 1955.

MacBryde, C. M. Signs and symptoms: applied pathologic physiology and clinical interpretation. 3 ed. etc. Philadelphia etc.: Lippincott (c 1957). Contains bibliogrs.

Mace, D. R. Marriage counselling: the first full account of the remedial work of the Marriage Guidance Councils. London: Churchill. 1948.

Master, A. M. Cardiac emergencies and heart failure: prevention and treatment by A. M. Master, M. Moser and H. L. Jaffe. 2 ed. thoroughly revised etc. Philadelphia: Lea & Febiger (c 1955 repr. 1956).

Maximow, A. A. A text-book of histology by A. A. Maximow and W. Bloom etc. 7 ed. Philadelphia: Saunders. 1957. Contains bibliogrs.

Meister, Alton. Biochemistry of the amino acids etc. N.Y.: Academic press. 1957. Contains bibliogrs.

Merton, R. K., ed. The student physician: Introductory studies in the sociology of medical education ed. by R. K. Merton, G. G. Reader and P. L. Kendall. Cambridge, Mass.: Published for the Commonwealth fund by Harvard University Press.

Moore, Thomas. Vitamin A etc. Amsterdam, London etc.: Elsevier. 1957. Contains bibliogrs.

Nabarro, J. D. N. Biochemical investigations in diagnosis and treatment etc. London: Lewis. 1954.

New York (State) University. Bureau of vocational curriculum development and industrial teaching training. Bacteriology for nurses. N.Y., Delmar. 1951.

Newman, Charles. The evolution of medical education in the nineteenth century by C. Newman etc. London: Oxford University. 1957.

Osborn, G. H. Synthetic ion-exchangers: recent developments in theory and application etc. London: Chapman & Hall. 1955.

Pannekoek, Ant. Anthropogenesis: a study of the origin of man etc. Amsterdam: North-Holland publishing co. 1953.

Parry, D. W. Mathematics of drugs and solutions in ten lessons by D. W. Parry etc. N.Y.: G. P. Putnam's sons (*c* 1954, repr. 1955).

Paterson, Donald. Pediatrics ed. by D. Paterson and J. F. McCreary etc. Philadelphia: Lippincott (*c* 1956). Contains bibliogrs.

Pedersen, Jorgen. Diabetes and pregnancy: blood sugar of newborn infants during fasting and glucose administration. Copenhagen: Danish Science Press. 1952.

Penicillin in severe otorhinolaryngological complications: a symposium decided by Robert Lund and others. Copenhagen: Danish-Norwegian-Swedish otolaryngological joint research. 1950.

Peplau, H. E. Interpersonal relations in nursing: a conceptual frame of reference for psychodynamic nursing by H. E. Peplau. N.Y.: Putnam's sons (*c* 1952).

Pieters, H. A. J. Safety in the chemical laboratory by H. A. J. Pieters and J. W. Creyghton. 2 ed. London: Butterworth. 1957.

Piulachs, P. Ulcers of the legs by P. Piulach etc. Springfield, Illinois: Charles C. Thomas (*c* 1956). Contains bibliogr.

Prince, J. H. Comparative anatomy of the eye. Springfield, Illinois: Charles C. Thomas (*c* 1956).

Rabinowitch, E. I. Photosynthesis and related processes etc. N.Y.: Interscience. 1945. 3 v. in 2.

Rebuck, J. W. The leukemias: etiology, pathophysiology, and treatment ed. by J. W. Rebuck, F. H. Bethell and R. W. Monto etc. N.Y.: Academic Press. 1957. Contains bibliogrs. (Henry Ford Hospital—International symposium.)

Romer, A. S. Osteology of the reptiles etc. Chicago: University of Chicago (*c* 1956).

Ruskin, Arthur. Classics in arterial hypertension by A Ruskin etc. Springfield, Illinois: Charles C. Thomas. 1956.

Russell, Bedford. The nasal aspect of migraine, etc. Bristol: Wright. 1955. Publ. in an abridged form in the Proceedings of the Royal Society of Medicine, February 4, 1955.

Schnitzer, R. J. Drug resistance of microorganisms by R. J. Schnitzer and E. Grunberg etc. N.Y.: Academic press. 1957.

Sebrell, W. H., ed. The vitamins: chemistry, physiology, pathology ed. by W. H. Sebrell and R. S. Harris etc. N.Y.: Academic press. 1954. 3 v.

Short, C. L. Rheumatoid arthritis: a definition of the disease and a clinical description based on a numerical study of 293 patients and controls by C. L. Short, W. Bauer and W. E. Reynolds etc. Cambridge, Mass.: Harvard University. 1957.

Sollmann, Torald. A manual of pharmacology. 8 ed. London: Saunders. 1957.

Spink, W. W. The nature of brucellosis. Minneapolis: University of Minnesota (*c* 1956).

Stefanini, Mario. The hemorrhagic disorders: a clinical and therapeutic approach by M. Stefanini, W. Dameshek etc. N.Y. etc.: Grune & Stratton. 1955.

Stimson, P. M. A manual of the common contagious diseases by P. M. Stimson and H. L. Hodes. 5 ed. rev. etc. Philadelphia: Lea & Febiger. 1956. Contains bibliogrs.

Thompson, R. H. S. Biochemical disorders in human disease ed. by R. H. S. Thompson and E. J. King etc. London: Churchill. 1957. Contains bibliogrs.

Tocantins, L. M., ed. Progress in hematology. N.Y.: Grune & Stratton. 1956. Contains bibliogrs. Library has vol. 1.

Todd, Sir Alexander, ed. Perspectives in organic chemistry. N.Y.: Interscience publishers. 1956. Contains bibliogrs.

Tullis, J. L., ed. Blood cells and plasma proteins: their state in nature. N.Y.: Academic press. 1953. Contains bibliogrs. (Memoirs of the University Laboratory of Physical Chemistry related to Medicine and public health. Harvard University No. 2.)

Waelsch, Heinrich, ed. Biochemistry of the developing nervous system: proceedings of the first International Neurochemical Symposium, held at Magdalen College, Oxford, July 13-17, 1954, ed. by H. Waelsch etc. N.Y.: Academic press. 1955. Contains bibliogrs.

Werner, S. C., ed. The thyroid: a fundamental and clinical text ed. by S. C. Werner etc. London etc.: Cassell (*c* 1955). (Contains bibliogrs.)

Whistler, R. L. Polysaccharide chemistry by R. L. Whistler and C. L. Smart etc. N.Y.: Academic press. 1953. Contains bibliogrs.

White, J. E. M. Anthropology by J. E. Manchip White etc. London: English Universities Press. 1954.

White, Lynn., ed. Frontiers of knowledge in the study of man etc. N.Y.: Harper (*c* 1956).

White, P. D. Clues in the diagnosis and treatment of heart disease; 2 ed. by P. D. White etc. Springfield, Illinois: Charles C. Thomas. 1956. (American Lecture Series No. 295—Monograph in the Bannerstone Division of American lectures in circulation.)

Williams, D. R. Administration of schools of nursing by D. R. Williams ed. by I. M. Stewart etc. N.Y.: Macmillan. 1950. Contains bibliogrs.

Witschi, Emil. Development of vertebrates. Philadelphia etc. Saunders. 1956.

Wolf, Stewart. The evaluation of therapeutic agents with special reference to the tranquilizing drugs, etc. Washington: American Psychiatric Association (*c* 1957). (American Psychiatric Association Mental Hospital service. Monograph 2.)

Wolf-Heidegger, Gerhard. Atlas of systematic human anatomy. Edinburgh: Livingstone. 1957. Library has v. 1 and 3.

Woods, A. C. Endogenous uveitis, with illustrations by A. S. Burgess etc. Baltimore: Williams & Wilkins. 1956.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

KAOPECTATE (UPJOHN) AND KAOPECTATE WITH NEOMYCIN

These products are handled by Westdene Products (Pty.) Ltd., who supply the following information:

Kaopectate is a combination of kaolin with pectin in a pleasantly flavoured vehicle. The kaolin in this combination has many advantages in the treatment of non-specific diarrhoeas. It is free from impurities normally found in commercial kaolin, and is, therefore, well tolerated. Its minute particle size enhances its adsorption and protective qualities.

Kaopectate with Neomycin is used in the treatment of diarrhoea. Each fluid ounce of Kaopectate with Neomycin contains 300 mg. of Neomycin sulphate, 5·832 g. (90 gr.) of kaolin, and 0·130 g. (2 gr.) of pectin suspended with methylcellulose 1·25%. Kaopectate with Neomycin is a palatable, aqueous preparation of the wide-spectrum antibiotic, Neomycin sulphate in a remarkably stable suspension of kaolin and pectin suspended with methylcellulose. Kaolin and pectin are capable of removing bacteria and irritants that are common causes of diarrhoea and of protecting the intestinal mucosa against certain irritating substances. The action of kaolin is purely mechanical. Through its surface action bacteria, toxins and irritants are absorbed. Kaopectate products have exceptional absorptive properties (different grades and types of kaolin vary in this regard). Since kaolin, pectin, methylcellulose and Neomycin are not absorbed from the intestinal tract, Kaopectate with Neomycin acts entirely within the bowel, removing or destroying the inciting irritants, while serving to protect the intestinal mucosa and reducing the inflammatory process present. It does not interfere with the action of the gastric or intestinal contents and promotes the return of formed stools.

Packs. Kaopectate in 6 fl. oz. bottles. Keopectate with Neomycin in 4 fl. oz. bottles.

PASSING EVENTS : IN DIE VERBYGAAN

The Professional Provident Society of South Africa achieved two milestones in its development during October 1957. Its assets passed the quarter million mark and its membership rose to over one thousand. This Society, which is run by the professions for their members, is offering substantial benefits to its members.

* * *

Dr. O. S. Treisman, M.B., B.Ch. (Rand), M.R.C.O.G. has commenced practice as a specialist Gynaecologist and Obstetrician at 1008 Cavendish Chambers, Jeppe Street, Johannesburg. Telephones (which do not appear in the current issue of the telephone directory): Rooms 22-3216, residence 44-5755, emergency 22-4191.

* * *

Medico-Surgical Cinema. The annual prize of 100,000 Frs. cash and other awards will be given during the last session of the course of 'Actualités Medico-Chirurgicales' at the 'Faculté de Médecine de Paris' in March 1958. The jury will consider the didactic value of the film as well as its cinegraphic quality. Only 16 mm. film will be admitted. Applications and films are to be sent to the office of the journal *La Presse Médicale*, 120 Boulevard Saint Germain, Paris VI° before 15 February 1958. Contrary to the precedent of former years subsidized films, or those produced by a laboratory or firm are eligible for competition.

* * *

The Fourth Internationale Goitre Conference, organized by the American Goiter Association and the London Thyroid Club will take place in London on 5-9 July 1960. It will precede the International Endocrine Conference in Copenhagen by 10 days. Scientific sessions will be held under the presidency of Sir Charles Harington, F.R.S., at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2 on 6-8 July. The registration fee is £4 sterling or $10 U.S. The proceedings will be published in English, French, Spanish and German. Abstracts of papers for consideration by the Programme Committee must be sent not later than 31 December 1959 to Dr. Selwyn Taylor, 3 Roedean Crescent, London, S.W. 15, or Dr. John C. McClintock, 149½ Washington Avenue, Albany 10, N.Y., U.S.A. Hotel reservations may be secured from Messrs. Thomas Cook & Sons Limited, and it is expected that special facilities for travel will be offered by B.O.A.C. A few honoraria will be available for travel expenses, about which enquiries may be made to either of the above mentioned.

REVIEWS OF BOOKS : BOEKRESENSIES

THE ROYAL CANADIAN ARMY MEDICAL CORPS

Official History of the Canadian Medical Services 1939–1945. Volume One—Organization and Campaigns. Edited by W. R. Feasby, B.A., M.D. Maps drawn by Captain C. C. J. Bond. Pp. xii + 568. 8 Charts. 48 Illustrations. $5·00. Ottawa: Queen's Printer and Controller of Stationery. 1956.

Contents: 1. The Military Medical Service on the Eve of War. 2. Mobilization Plans. 3. The First Months of War. 4. The Canadian Scene. 5. The R.C.A.M.C. n Britain. 6. Hospital Policy Overseas. 7. The Dieppe Raid. 8. The Sicilian Campaign. 9. Southern Italy. 10. The Liri Valley. 11. Advance to the Senio. 12. The Invasion of Normandy. 13. The Normandy Battles. 14. The Breakout and Pursuit. 15. Opening the Port of Antwerp, and the Winter on the Maas. 16. The Rhineland Offensive. 17. The Final Phase and Occupation. 18. Hong Kong. 19. Ancillary Medical Services for the Army. 20. The Medical Branch of the Royal Canadian Navy. 21. The Development of the R.C.A.F. Medical Branch. 22. Medical Arrangements for the British Commonwealth Air Training Plan. 23. Medical Statistics—B.C.A.T.P. Personnel. 24. Special Functions of the R.C.A.F. Medical Branch. 25. Observations on the R.C.A.F. Medical Branch. 26. The Canadian Dental Corps. 27. Manpower and the Medical Services. 28. The Canadian Medical Procurement and Assignment Board. 29. Civil Defence. 30. The Department of National Health and Welfare, 1939—1945. 31. The Canadian Red Cross Society. 32. The St. John Ambulance.

The story of the Canadian Medical Services contained in this volume is one of fantastic achievement. It tells how a small permanent force of the R.C.A.M.C. rapidly developed into a large efficient service which ministered to (*a*) The Army at home and in the field. (*b*) The Royal Canadian Air Force. (*c*) The Royal Canadian Navy, and (*d*) the Commonwealth Air Training Scheme. As end products of this expansion, the Canadian Armed Forces are left today with separate medical services for the Army, the Navy and Air Force.

The early chapters describe the problems relating to mobilization and hospitalization at home; this is followed by a description of the despatch of the Expeditionary Force to the European Theatre of War. And how, on its arrival in Britain it became obvious that major reorganization would be necessary to meet a new type of warfare in which mobility had become the keynote. A summary of the revolutionary changes which were suggested by the Hartgill Committee make interesting reading. So, too, do the Canadian counter proposals.

Following the fall of France, the Canadian Force was obliged to play a purely defensive role while in Britain. Nevertheless, the Allies were committed to an invasion of the Continent of Europe, to which the Canadian contribution was to be about 185,000 men. To meet the requirements of this force 23,000 General Hospital beds were made available.

The next section of this Official History contains a description of the several campaigns in which the Canadians were involved—The Dieppe Raid, the Sicilian Landings, the Advance in Southern Italy and finally Normandy and the Rhineland battles. The Medical Plan for each is given together with an account of the training involved. The actual operations are clearly illustrated with excellent maps and diagrams, which are of great assistance when following descriptions of the medical arrangements.

A record of the work done by the Nursing Services reminds us of the 300 Canadian trained nurses who saw service with the South African Military Nursing Service in the Union, Middle East, North Africa and Italy.

This History contains much that will interest Medical Officers who served in the same theatres as the Canadians. It is however, to the student of Military Medicine that it will have its biggest appeal. The many problems faced by the Canadian Medical Authorities in 1939 were so similar to those of the Union, both countries having to maintain large Expeditionary Forces a long distance from Home Base, that much can be learnt from a comparison of the methods adopted by each. The volume should be available in every Military Academy.

R.L.F.

ORTHOPAEDIC GYMNASTICS

Orthopädische Gymnastik. Third Edition. Prof. Dr. Hohmann and L. Jegel-Stumpf. Pp. xvi + 138. 217 Illustrations. DM 19.50. Stuttgart: Georg Thieme Verlag. 1956.

Contents: Zum Geleit. Vorwort zur ersten Auflage. Vorwort zur zweiten Auflage. Vorwort zur dritten Auflage. Wesen und Wege der Heilgymnastik. Allgemeine Grundlagen für die Durchführung der orthopädischen Übungen. Verbotene Gewohnheiten. *Der runde Rücken:* Verbotene Übungen. Rundrückenübungen im Liegen, im Sitzen, im Hängen, im Knien, im Stehen und Gehen. *Die Lordose:* Lordosenübungen im Liegen, im Hängen, im Sitzen, im Knien, im Stehen und Gehen. *Der flache Rücken:* Flachrückenübungen in Bauchlage, in Rückenlage, im Hängen, im Sitzen, im Kriechen, im Kniestand, im Stehen und Gehen. *Die Skoliosen.* Skoliosenübungen in Bauchlage, in Rückenlage, in Seitenlage, im Hängen, im Sitzen, im Kriechen, im Stehen und Gehen. *Leistungsstörungen an Arm und Bein:* Lähmungen. Gelenkkontrakturen. Fehlformen (X-, O-Bein usw.) Fehlform und Leistungsstörung des Fusses. Kreislaufstörungen am Bein. Gebrauchsstörungen an Hand und Fingern. Nachbehandlung von Verletzungen der Gliedmassen. Übungen an Hand und Arm. Übungen an Fuss und Bein. X-Bein-Übungen. O-Bein-Übungen. Dehnung von Kontrakturen. Nachwort Literatur.

This is a concise and useful treatise on orthopaedic gymnastics that should be a guide to the expert as well as the busy general practitioner. It begins with a few pages on curative gymnastics. Then, with the usual German thoroughness, some pages are devoted to the general principles of orthopaedic exercises and contra-indications. It deals in a practical manner with back anomalies such as lordosis, scoliosis, kyphosis and indeed any other conditions which the specialist in Physical Medicine and the G.P. will ordin-

arily encounter in their consulting rooms. The methods of treatment are effective and up-to-date, and when judiciously applied should be invalubale in expediting rehabilitation.

For those not conversant with German many of the exercises are well-illustrated and self-explanatory. This little volume deserves the highest recommendation.

W.C.H.

BLOOD GROUP SEROLOGY

An Introduction to Blood Group Serology. By Kathleen E. Boorman, Senior Scientific Officer, South London Blood Transfusion Centre and Barbara E. Dodd, M.Sc. (Lond.), Ph.D. (Lond.). Pp. viii + 317. 30 illustrations. 40s. net. London: J. & A. Churchill, Ltd.

Contents: I. Introduction. II. The ABO Blood Group System. III. The Rh Blood Group System. IV. Other Blood Group Systems. V. Practical Applications of Blood Group Theory. VI. Apparatus and Reagents. A Practical Guide to Laboratory Procedure. Glossary. Numerical Index of Techniques.

Although this book is intended primarily for blood transfusion technicians, it contains a great deal of useful technical information for the more advanced worker. Unfortunately, many basic aspects of the subject are dealt with in an entirely perfunctory and inadequate manner. For example, a one-to-one correspondence between gene, antigen and antibody is postulated by the authors as the basis of all blood grouping techniques. This is an obvious over-simplification of the truth, ignoring as it does both Landsteiner's classic definition of serological specificity as the 'disproportionate action of a number of similar agents on a variety of related substrata' and Wiener's penetrating distinction between blood factors and agglutinogens. Again, Wiener's theory of multiple allelomorphism as the pattern of inheritance of the Rh, MNS and other blood group systems, which is fundamental to an understanding of the serology and genetics of the blood group which has never been disproved and which is accepted by many if not most of the foremost authorities in the blood grouping field (whatever reservation some may have regarding his nomenclature) is not even mentioned. Instead, the reader is left with the impression that the genetics of the Rh system were discovered by Fisher and that his theory of closely linked genes is the first and last word on the subject.

On the practical side, the techniques described are based almost exclusively on prolonged incubation of serum-cell mixtures in precipitin tubes, great stress being laid on dexterity in the use of the Pasteur pipettes to transfer the cell deposits to slides for microscopic examination. The only use which the authors can find for the laboratory centrifuge is for packing and washing cells. They ignore the fact that centrifugation techniques are employed in many highly reputable blood grouping laboratories throughout the world with as great precision as those claimed for the methods described and with the added advantages of reduction in time and accentuation of agglutination reactions—factors which are of the utmost importance in any efficiently organised blood transfusion laboratory. The equipment and cleaning methods described and illustrated in the section on Blood Transfusion Apparatus are those still in use in the National Blood Transfusion Service in England. For many, this section will serve only as a grim reminder of the old 'bottle-washing days' of blood transfusion practice, long since superseded by the use of commercially prepared sterile, apyrogenic, disposable blood bottles, giving sets and taking sets which have done so much to make blood transfusion safer and more comfortable for the patients.

M.S.

TROPICAL DISEASES

Lehrbuch der Tropenkrankheiten. By Ernst Georg Nauck. Pp. VIII + 432. 125 Illustrations. DM 64.–. Stuttgart: Georg Thieme Verlag. 1956.

Contents: Arthropoden als Krankheitserreger und -überträger. Durch Würmer verursachte Krankheiten. Durch Protozoen verursachte Krankheiten. Durch Spirochaeten verursachte Krankheiten. Durch Bakterien verursachte Krankheiten. Rickettsiosen. Tropische Viruskrankheiten. Durch Pilze verursachte Krankheiten. Auf Ernährungsschäden zurückgeführte Krankheiten. Krankheiten verschiedener Ätiologie. Gifttiere. Sachregister.

The Medical School of the University of Hamburg and the renowned institute of Tropical Medicine of that city have always been regarded as one of the chief centres for the dissemination of knowledge of tropical diseases amongst German-speaking peoples. The textbook under review, written by Professor Nauck and his colleagues aims at re-establishing that tradition after a lapse of many years.

The book is of modest dimensions and is to be regarded as an introduction to more detailed study; it serves, I should say, as an admirable medium for the German-speaking medical student and general practitioner to acquire a good working knowledge of the present-day advances in this field. In the 412 pages the authors purvey a great detail of information.

The different diseases are grouped under headings indicating the causative factor or vector. Thus we find a large section devoted to diseases caused by worms. Then in order, diseases caused by protozoa, by spirochaetes, by bacteria, by ricketssia, by viruses and by fungi. Other sections comprise illnesses due to malnutrition such as kwashiorkor and sprue. In a special section we find trachoma, lymphogranuloma inguinale, which is a virus disease, and granuloma inguinale, which is a bacterial disease. Finally, there is a special chapter on diseases caused by poisonous agents such as snakes, scorpions and spiders.

The book begins with a detailed consideration of those arthropods which cause or convey disease to man. This part is very thoroughly done. The anatomy, habits and geographic dissemination of the various members of the arthropoda are concisely described and the numerous tables show the relationship between the various subdivisions in this immense class of living creatures. This section ends with a review of the latest methods of protecting the individual from disease-bearing insects and includes a discussion on general environmental measures and the value of the latest insecticides.

As the notice on the jacket points out, many therapeutic advances have been made since the last edition of a German textbook on tropical diseases appeared in 1942. In this volume the gap has been bridged and the text reflects this progress. Important diseases such as amoebiasis, malaria, hookworm disease and bilharzia receive a large share of the authors' attention. In this, as indeed in all the other diseases described, the life-history of the causative agent, the clinical symptoms and the recommended general prophylactic measures are adequately described. It is noteworthy from a perusal of the text that Germany herself has made little or no contribution to the newer therapeutic armamentarium in tropical medicine. But all the newer drugs are discussed and evaluated. What illustrations there are, are good. But there are not as many as in a well-known standard English text-book on the same subject. On the other hand the illustrations in this volume are new. They have not appeared in previous editions and have the attraction of a first appearance. No doubt in the future editions of this book (and one feels that it is going to become a favourite and remain so for many years) there will be many additions both of photographs of actual cases and illustrative diagrams.

The format, printing and general physical characters of this handy volume are in keeping with the excellent standard of this firm's publications. It is, for its size, well stocked with up-to-date information and it should prove a 'best-seller' on this subject amongst German-speaking students and practitioners. There is no need however for the English reader to go to it as a source of information.

C.K.O.'M.

RELAXATION IN CHILDBIRTH

Relaxation and Exercise for Natural Childbirth. By Helen Heardman. Pp. 32. 22 Figures. 1s. net + 3d. postage abroad. Edinburgh & London: E. & S. Livingstone Ltd. 1956.

Contents: I. Relaxation and Exercise for Natural Childbirth. II. Labour.

This little book is written by a physiotherapist. The text is devoted to a description of relaxation technique and exercises to ensure, as far as possible, a reasonably painless labour. There is also a short chapter on normal labour and the application of the exercises to it.

This inexpensive book can confidently be recommended to pregnant mothers.

E.M.S.

AIDS TO OPHTHALMOLOGY

Aids to Ophthalmology Eleventh Edition. By P. McG. Moffat, M.D. (Lond.), M.R.C.P., F.R.C.S. (Eng.), D.O.M.S. Pp. 282. Illustrated. 10s. 6d. London: Baillière, Tindall & Cox Ltd. 1957.

Contents: Introduction. The Examination of the Eye. Bacteriology. The Conjunctiva. Conjunctivitis. Diseases of the Lids. Lacrimal Diseases. Diseases of the Orbit. Diseases of the Sclera. Corneal Ulcers. Interstitial Keratitis. Other Corneal Disorders. Diseases of the Uveal Tract. Diseases of the Iris. Glaucoma. Diseases of the Choroid. Diseases of the Vitreous. Diseases of the Optic Nerve and Retina. Cataract. Injuries to the Eye. Refraction. Objective Determination of Refraction. Subjective Determination of Refraction. Prescribing Glasses. Myopia. The Fitting of the Glasses. Examples in Refraction. Squint. Muscle Balance and Convergence. Disorders of Accommodation. Paralysis of the External Muscles of the Eye. Amblyopia, Retinal and Cerebral. Hemianopsia. Eye Signs of Body Disease. Ocular Therapeutics. Operations. War Injuries. Eye Conditions in School Children. The Blind. Standards of Vision. Examination Questions. Index.

The 'Aids' series have proved their popularity in the fact that the first edition of the volume on Ophthalmology was first issued in 1908 and has now entered its 11th edition, brought up to date and revised by its present author. In the vast subject Ophthalmology has developed into, as can be seen from the list of chapters, the problem is how to cover the subject matter adequately and while avoiding being just a mass of dry facts for memorizing, still be readable. In this difficult problem of balance, the author has admirably succeeded. Unavoidably, certain important subjects have suffered from excessive compression, e.g. proptosis is discussed in a matter of six lines. Again, other facts may have to be omitted. (One gross omission is the treatment of simple corneal ulcers.) It is noted that the author does not follow the American system of classification of uveitis into granulomatous and non-granulomatous types, or of glaucoma into narrow and open-angle types. Nor does he use steroids for treating phlyctenular disease, which has proved so successful in South Africa. It is interesting to note the extreme frequency of application of penicillin drops in gonococcal ophthalmia neonatorum. The author considers that trachomatous pannus is a result of the irritation of the cornea by the rough lids. Duke-Elder has stated that the inflammation of this tissue is 'specific and primary and not secondary and incidental'.

Despite these minor criticisms, this booklet which is of a convenient size to fit into one's pocket, should be of assistance in being an 'Aid' to the student in getting at the bones of the subject, which in the lecture room and clinic tends to be lost amidst a clutter of information and a welter of words.

S.L.L.

CORRESPONDENCE : BRIEWERUBRIEK

SURVIVAL AT SEA

To the Editor: In your Editorial[1] under this title in the *Journal* of 26 October you recommend that drinking of sea water must be forbidden and that owing to its unfavourable composition juice obtained from fish should also not be taken. Fish as a food you stated, should be avoided in the absence of abundant fresh water.

This was the universally accepted view, until Dr. Bombard[2] dared to suggest that sea water and fish juice could sustain life. To prove his theory, this courageous man drifted alone across the Atlantic Ocean in a rubber dinghy, taking 65 days to cross from the Canaries to the West Indies.

That he survived one of the most dramatic and drastic experiments in the history of medicine, is surely proof enough even for the most sceptical.

Mariners would be well advised to heed the opinion of one who has survived what they themselves may be called upon to suffer.

H. M. Selvey

P.O. Box 423
Salisbury
Southern Rhodesia

25 November 1957

1. Editorial (1957): South African Medical Journal. **31**, 1084.
2. Bombard A. (1953): *The Bombard Story*. London: A. Deutch. (Penguin Books 1956)

INCIDENCE OF DIABETES MELLITUS IN THE BANTU

To the Editor: In his article on urinary oestrogen levels in the *Journal* of 16 November, Dr. I. Bersohn, during discussion of 'disease pattern' differences in the Bantu and European, includes diabetes amongst the diseases which have a low incidence among the Bantu. While the incidence may be lower than in the White population, the infrequency is not of the same order as that of peptic ulceration or cholelithiasis, as seems implied.

In 1956, of a total of 37,786 admissions to Baragwanath Hospital, 153 admissions were for diabetes mellitus and only 55 for peptic ulcers. It is predictable that diabetes will be less common in the Bantu than, for example, in the United States population, because of the different age-structure of the two groups. The Bantu on the average dies earlier, thus reducing the number of diabetics in the older age-groups where the bulk of American diabetics are found.

Diabetes in the Bantu is so common a clinical problem at this hospital that the institution of a diabetic clinic is contemplated. The treatment of patients of little education, living on a predominantly carbohydrate diet, poses special problems in the effective control of the disease. In one of 4 medical units, each of 80 beds, 28 new cases of diabetes per year have, on the average, been seen over the past 3 years.

Finally, the influence of Bantu siderosis on the incidence of diabetes is as yet unknown; it might be expected to operate as an aggravating factor, becoming increasingly important the longer the individual lives.

K. J. Keeley
Physician

Department of Medicine
Baragwanath Hospital
Johannesburg

25 November 1957

PROTECTION FOR FULL-TIME MEDICAL PERSONNEL

To the Editor: A few months ago the Federal Council considered the question of the protection of full-time medical personnel, particularly those employed in the Government Service. The matter was referred to the Central Health Services and Hospitals Coordinating Council, on which the Central Government and the Provincial Administrations are represented as constituent bodies.

I have now received a letter from the Secretary of that Council which states:

> 'The Council, at its thirty-third meeting, having considered these comments, resolved as follows: "That the Medical Association of South Africa be informed that the contents of their letter were referred to the constituent bodies, who have commented that their medical personnel are not insured against any civil actions which might be brought against them. They accept their own liability."'

In the circumstances I would advise all full-time medical officers who are employed by these Administrations to see that they are adequately protected against any civil actions which might be brought against them as a result of the exercise of their profession.

The Association has made arrangements with two organizations to provide protection—the Medical Protection Society of London and the Atlas Assurance Company. Further information may be obtained from the Association's Office, P.O. Box 643, Cape Town.

A. H. Tonkin
Secretary

Medical Association of South Africa
Medical House
35 Wale Street
Cape Town

4 December 1957